

=> d his

(FILE 'HOME' ENTERED AT 19:54:09 ON 13 SEP 2006)

FILE 'REGISTRY' ENTERED AT 19:54:19 ON 13 SEP 2006
L1 STRUCTURE UPLOADED
L2 50 S L1 SSS SAM

FILE 'HOME' ENTERED AT 19:55:41 ON 13 SEP 2006

FILE 'REGISTRY' ENTERED AT 20:03:37 ON 13 SEP 2006
L3 STRUCTURE UPLOADED

FILE 'HCAPLUS' ENTERED AT 20:04:03 ON 13 SEP 2006

FILE 'REGISTRY' ENTERED AT 20:04:13 ON 13 SEP 2006
L4 STRUCTURE UPLOADED
L5 50 S L4 SSS SAM

FILE 'HOME' ENTERED AT 20:05:51 ON 13 SEP 2006

FILE 'REGISTRY' ENTERED AT 20:09:46 ON 13 SEP 2006
L6 STRUCTURE UPLOADED
L7 46 S L6 SSS SAM

FILE 'HOME' ENTERED AT 20:12:35 ON 13 SEP 2006

FILE 'REGISTRY' ENTERED AT 20:13:25 ON 13 SEP 2006
L8 STRUCTURE UPLOADED
L9 44 S L8 SSS SAM
L10 1034 S L8 SSS FULL

FILE 'HCAPLUS' ENTERED AT 20:15:09 ON 13 SEP 2006
L11 252 S L10
E HYPOCALCEMIA+ALL/CT
E HYPERCALCEMIA+ALL/CT
E HYPERPARATHYROIDISM+ALL/CT
L12 34 S L11 AND (HYPOCALCEMIA OR HYPERCALCEMIA OR (HYPERPARATHYROIDIS
L13 9 S L11 AND CALC?
L14 2 S L13 NOT L12

FILE 'HOME' ENTERED AT 20:24:53 ON 13 SEP 2006

FILE 'AGRICOLA, ALUMINIUM, ANABSTR, APOLLIT, AQUALINE, AQUIRE, BABS,
BIOTECHNO, CABA, CAOLD, CAPLUS, CBNB, CEABA-VTB, CERAB, CIN, COMPENDEX,
CONFSCI, COPPERLIT, CORROSION, DISSABS, ENCOMPLIT, GENBANK, INSPEC,
INSPHYS, INVESTEXT, IPA, JICST-EPLUS, KOSMET, ...' ENTERED AT 20:39:35 ON
13 SEP 2006

FILE 'AGRICOLA, ALUMINIUM, ANABSTR, APOLLIT, AQUALINE, AQUIRE, BABS,
BIOTECHNO, CABA, CAOLD, CAPLUS, CBNB, CEABA-VTB, CERAB, CIN, COMPENDEX,
CONFSCI, COPPERLIT, CORROSION, DISSABS, ENCOMPLIT, GENBANK, INSPEC,
INSPHYS, INVESTEXT, IPA, JICST-EPLUS, KOSMET, ...' ENTERED AT 20:39:50 ON
13 SEP 2006

FILE 'HCAPLUS' ENTERED AT 20:40:08 ON 13 SEP 2006
SET LINE 250
SET DETAIL OFF
E "193275-84-2"/BI,RN 25
SET NOTICE 1000 SEARCH
L15 175 S E3 OR E5 OR E6 OR E7 OR E8 OR E9 OR E10 OR E11 OR E12 OR E13
SET NOTICE LOGIN SEARCH
SET LINE LOGIN
SET DETAIL LOGIN

L16 555360 S L15 AND CAL? OR HYPER?
 L17 28 S L15 AND (CAL? OR HYPER?)

=> d l17 not l12
 L12 IS NOT VALID HERE
 For an explanation, enter "HELP DISPLAY".

=> s l17 not l12
 L18 9 L17 NOT L12

=> s l18 not l13
 L19 8 L18 NOT L13

=> d l19 ibib hitstr abs

L19 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2006:769235 HCAPLUS <<LOGINID::20060913>>
 DOCUMENT NUMBER: 145:202934
 TITLE: Farnesyltransferase inhibitors for treatment of
 laminopathies, cellular aging and atherosclerosis
 INVENTOR(S): Gordon, Leslie B.; Collins, Francis S.; Glover,
 Thomas; Glynn, Michael W.; Capell, Brian C.; Cox,
 Adrienne D.; Der, Channing J.
 PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA;
 Progeria Research Foundation; The Regents of the
 University of Michigan; The University of North
 Carolina at Chapel Hill
 SOURCE: PCT Int. Appl., 104pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006081444	A2	20060803	WO 2006-US2977	20060127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

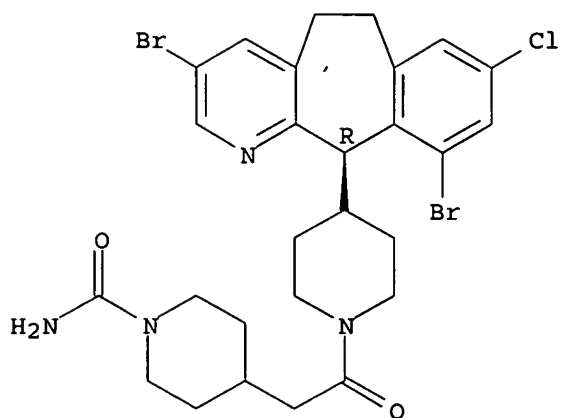
PRIORITY APPLN. INFO.: US 2005-648307P P 20050128
 US 2005-707192P P 20050809

IT 193275-84-2, Sarasar
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (farnesyltransferase inhibitors for treatment of laminopathies,
 cellular aging and atherosclerosis)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-
 5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB Although it can be farnesylated, the mutant lamin A protein expressed in Hutchinson-Gilford Progeria Syndrome (HGPS) cannot be defarnesylated because the characteristic mutation causes deletion of a cleavage site necessary for binding the protease ZMPSTE24 and effecting defarnesylation. The result is an aberrant farnesylated protein (called "progerin") that alters normal lamin A function as a dominant neg., as well as assuming its own aberrant function through its association with the nuclear membrane. The retention of farnesylation, and potentially other abnormal properties of progerin and other abnormal lamin gene protein products, produces disease. Farnesyltransferase inhibitors (FTIs) (both direct effectors and indirect inhibitors) will inhibit the formation of progerin, cause a decrease in lamin A protein, and/or an increase prelamin A protein. Decreasing the amount of aberrant protein improves cellular effects caused by and progerin expression. Similarly, treatment with FTIs should improve disease status in progeria and other laminopathies. In addition, elements of atherosclerosis and aging in non-laminopathy individuals will improve after treatment with farnesyltransferase inhibitors.

=> d 119 ibib hitstr abs 2-8

L19 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:196534 HCAPLUS <<LOGINID::20060913>>

DOCUMENT NUMBER: 145:23059

TITLE: A rapid and simple HPLC-UV method for the determination of inhibition characteristics of farnesyl transferase inhibitors

AUTHOR(S): Appels, Natalie M. G. M.; Tung, Kien-On; Rosing, Hilde; Schellens, Jan H. M.; Beijnen, Jos H.

CORPORATE SOURCE: Department of Pharmacy and Pharmacology, Slotervaart Hospital/The Netherlands Cancer Institute, Amsterdam, 1066 EC, Neth.

SOURCE: Biomedical Chromatography (2006), 20(2), 161-165
CODEN: BICHE2; ISSN: 0269-3879

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

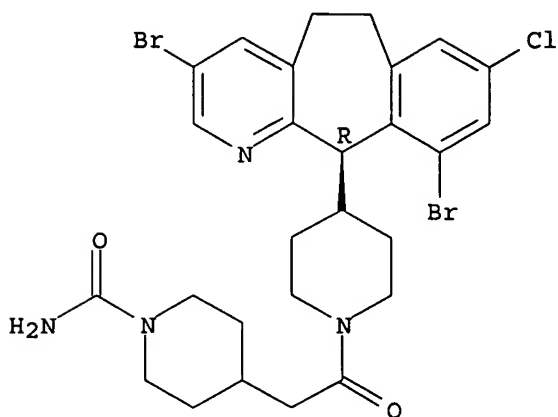
IT 193275-84-2, Lonafarnib

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(farnesyl transferase inhibitor screening by HPLC-UV)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB Ras proteins play an important role in the development of cancer. Farnesyl transferase inhibitors (FTIs) block the first obligatory post-translational step for activation, prenylation, of Ras proteins. To find new potent FTIs, rapid enzyme activity assays are required to reduce FTI development time. Most assays to date are based on radioactive labeled substrates. We developed a new, in vitro, farnesyl transferase assay based on gradient chromatog. coupled to UV detection. Unfarnesylated and farnesylated H-Ras proteins were resolved on a C18 wide-pore HPLC column and their concns. were determined with use of a calibration curve of unfarnesylated H-Ras. The assay was used to investigate inhibition characteristics of FTIs. The IC50 values of the FTIs L778,123 and SCH66336 were 4.2 nM and 78 μ M, resp. This assay could support the screening and development of FTIs to obtain rapid insights into their inhibitory properties.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:490384 HCAPLUS <<LOGINID::20060913>>
DOCUMENT NUMBER: 143:42681
TITLE: Anti-IGFR-1 antibodies in combination with chemotherapeutic agent for treating cancer
INVENTOR(S): Wang, Yan; Pachter, Jonathan A.; Bishop, Walter R.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005052005	A1	20050609	WO 2004-US38842	20041119
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,			

SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
 NE, SN, TD, TG

AU 2004292554	A1	20050609	AU 2004-292554	20041119
US 2005136063	A1	20050623	US 2004-993395	20041119
EP 1689782	A1	20060816	EP 2004-811545	20041119

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK,
 HR, IS, YU

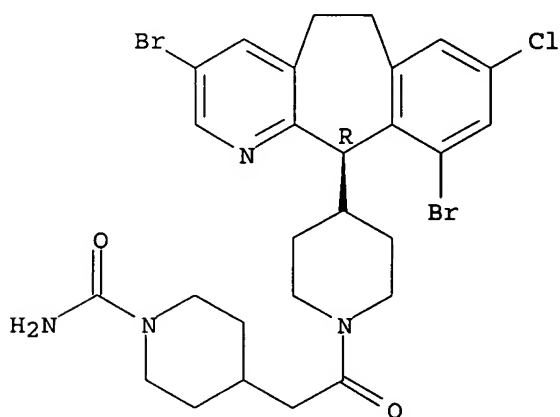
PRIORITY APPLN. INFO.: US 2003-524732P P 20031121
 WO 2004-US38842 W 20041119

IT 193275-84-2, Lonafernib
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (anti-IGFR-1 antibodies in combination with chemotherapeutic agent for
 treating cancer)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-
 5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB The present invention provides combinations including a binding composition, such as an anti-IGFR1 antibody, in association with a chemotherapeutic agent. The antibody is e.g. a human monoclonal antibody recognizing human IGFR-1, especially soluble IGFR-1. The chemotherapeutic agent is selected from a taxane, topoisomerase inhibitor, signal transduction inhibitor, cell cycle inhibitor, farnesyl protein transferase inhibitor, EGFR inhibitor, HER2 inhibitor, VEGFR inhibitor, MAP kinase inhibitor, MEK kinase inhibitor, AKT kinase inhibitor, mTOR inhibitor, etc. Methods for using the combinations to treat medical conditions, such as cancer, are also provided.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:369627 HCAPLUS <<LOGINID::20060913>>

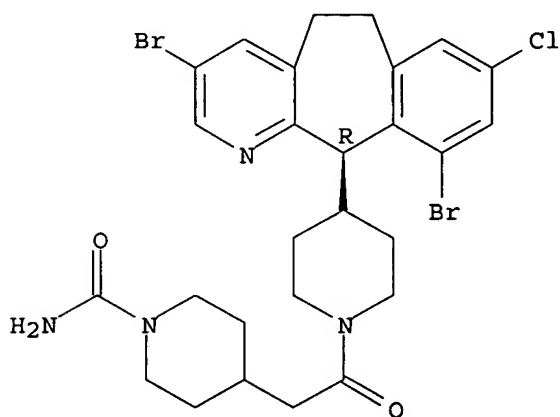
DOCUMENT NUMBER: 141:388236

TITLE: Phase I study of the farnesyltransferase inhibitor lonafernib with paclitaxel in solid tumors

AUTHOR(S): Khuri, Fadlo R.; Glisson, Bonnie S.; Kim, Edward S.; Statkevich, Paul; Thall, Peter F.; Meyers, Michael L.; Herbst, Roy S.; Munden, Reginald F.; Tendler, Craig; Zhu, Yali; Bangert, Sandra; Thompson, Elizabeth; Lu, Charles; Wang, Xue-Mei; Shin, Dong M.; Kies, Merrill S.; Papadimitrakopoulou, Vali; Fossella, Frank V.;

Kirschmeier, Paul; Bishop, W. Robert; Hong, Waun Ki
 CORPORATE SOURCE: Winship Cancer Institute, Emory University, Atlanta, GA, 30322, USA
 SOURCE: Clinical Cancer Research (2004), 10(9), 2968-2976
 CODEN: CCREF4; ISSN: 1078-0432
 PUBLISHER: American Association for Cancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 193275-84-2, Lonafarnib
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (recommended dose of farnesyltransferase inhibitor lonafarnib was 100mg p.o. twice daily with 175 mg/m2 of paclitaxel i.v. every three weeks in patients with solid tumors and encouraging clin. activity observed with combination regimen)
 RN 193275-84-2 HCAPLUS
 CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB To establish the maximum tolerated dose of lonafarnib, a novel farnesyltransferase inhibitor, in combination with paclitaxel in patients with solid tumors and to characterize the safety, tolerability, dose-limiting toxicity, and pharmacokinetics of this combination regimen. In a Phase I trial, lonafarnib was administered p.o., twice daily (b.i.d.) on continuously scheduled doses of 100 mg, 125 mg, and 150 mg in combination with i.v. paclitaxel at doses of 135 mg/m2 or 175 mg/m2 administered over 3 h on day 8 of every 21-day cycle. Plasma paclitaxel and lonafarnib concns. were collected at selected time points from each patient. Twenty-four patients were enrolled; 21 patients were evaluable. The principal grade 3/4 toxicity was diarrhea (5 of 21 patients), which was most likely due to lonafarnib. dose-limiting toxicities included grade 3 hyperbilirubinemia at dose level 3 (100 mg b.i.d. lonafarnib and 175 mg/m2 paclitaxel); grade 4 diarrhea and grade 3 peripheral neuropathy at dose level 3A (125 mg b.i.d. lonafarnib and 175 mg/m2 paclitaxel); and grade 4 neutropenia with fever and grade 4 diarrhea at level 4 (150 mg b.i.d. lonafarnib and 175 mg/m2 paclitaxel). The maximum tolerated dose established by the continual reassessment method was lonafarnib 100 mg b.i.d. and paclitaxel 175 mg/m2. Paclitaxel appeared to have no effect on the pharmacokinetics of lonafarnib. The median duration of therapy was eight cycles, including seven cycles with paclitaxel. Six of 15 previously treated patients had a durable partial response, including 3 patients who had previous taxane therapy. Notably, two of five patients with taxane-resistant metastatic non-small cell lung cancer

had partial responses. When combined with paclitaxel, the recommended dose of lonafarnib for Phase II trials is 100 mg p.o. twice daily with 175 mg/m² of paclitaxel i.v. every 3 wk. Addnl. studies of lonafarnib in combination regimens appear warranted, particularly in patients with non-small cell lung cancer.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:145717 HCAPLUS <<LOGINID::20060913>>

DOCUMENT NUMBER: 141:184712

TITLE: In vitro study of farnesyltransferase inhibitor SCH 66336, in combination with chemotherapy and radiation, in non-small cell lung cancer cell lines

AUTHOR(S): Loprevite, Maura; Favoni, Roberto E.; De Cupis, Alessandra; Scolaro, Tindaro; Semino, Claudia; Mazzanti, Paola; Ardizzoni, Andrea

CORPORATE SOURCE: Medical Oncology A, Unit, National Institute for Cancer Research, Genoa, I-16132, Italy

SOURCE: Oncology Reports (2004), 11(2), 407-414

CODEN: OCRPEW; ISSN: 1021-335X

PUBLISHER: Oncology Reports

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 193275-84-2, SCH 66336

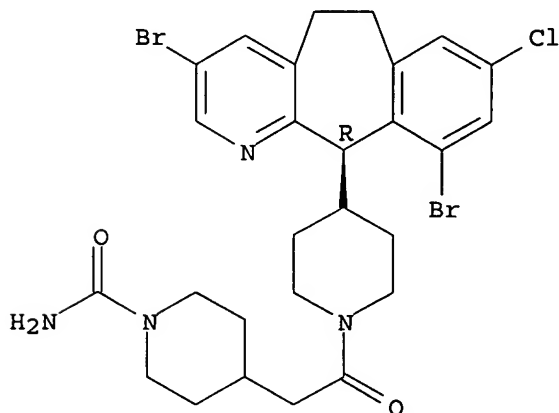
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(FTi SCH 66336 showed dose dependent cytostatic antitumor activity and dose dependent synergism in combination with antimitotic agent paclitaxel in NSCLC cell lines A-549, LX-1, CaLu-6 in vitro)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB K-ras alterations have been reported in 20-30% of non-small cell lung cancer (NSCLC) and represent a suitable target for the development of novel anticancer agents, such as Farnesyl transferase inhibitors (FTi), a new class of agents inhibiting the post-translational modification of the K-ras proteins. The effectiveness of FTi SCH66336 in inhibiting cell proliferation and deranging cell cycle of NSCLC cell lines as well as its interaction with chemotherapy or radiation have been evaluated. The activity of FTi SCH66336, alone or in combination with paclitaxel, gemcitabine, and radiotherapy, was examined in 3 cell lines, A-549, LX-1 and

CaLu-6, by colorimetric MTT assay. Cell cycle perturbation and apoptosis were also assessed by cytofluorimetric anal. The activity of SCH 66336 was found to be concentration- and time-dependent. The effect of SCH 66336, as demonstrated by cell growth recovery expts., resulted cytostatic and it was superimposable in both cell lines bearing 2 different K-ras mutations (A-549 and LX-1) and in K-ras wild-type Ca-Lu-6. In all cell lines the combination of SCH 66336 and paclitaxel resulted in a synergism of action when SCH 66336 followed paclitaxel treatment, whereas, antagonism was found when SCH 66336 preceded paclitaxel treatment. No significant synergism or addition with SCH 66336 followed by radiation treatment was noted. Different cell cycle phase blocks at various drug concns. were observed. In conclusion, SCH 66336 displays concentration-dependent cytostatic antitumor activity and schedule-dependent synergy with 2 commonly used anticancer agents in NSCLC cell lines. Further clin. testing of these combinations is warranted.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2000:314549 HCAPLUS <<LOGINID::20060913>>
 DOCUMENT NUMBER: 132:343356
 TITLE: A prenyl-protein transferase inhibitor for treating endometriosis
 INVENTOR(S): Oliff, Allen I.; Gibbs, Jackson B.
 PATENT ASSIGNEE(S): Merck & Co., Inc., USA
 SOURCE: PCT Int. Appl., 365 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000025789	A1	20000511	WO 1999-US25001	19991025
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 1998-106179P P 19981029
 GB 1999-160 A 19990105

OTHER SOURCE(S): MARPAT 132:343356

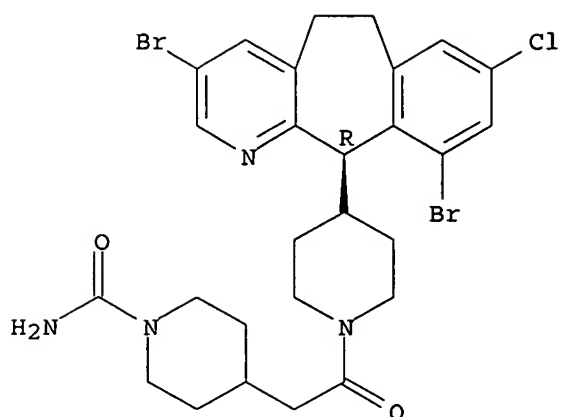
IT 193275-84-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (protein prenyltransferase inhibitors for treatment of endometriosis and related disorders)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB A method of preventing and treating endometriosis, uterine fibroids, dysfunctional uterine bleeding and endometrial hyperplasia is disclosed which is comprised of administering to a mammalian patient in need of such treatment an effective amount of a prenyl-protein transferase inhibitor. Various in vitro inhibition assays for farnesyltransferase were developed and effect of a prenyl-protein transferase inhibitor (5-160 mg/kg/day) was evaluated in vitro in the rat model of endometriosis.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:337641 HCAPLUS <<LOGINID::20060913>>

DOCUMENT NUMBER: 131:124925

TITLE: Tricyclic Farnesyl Protein Transferase Inhibitors: Crystallographic and Calorimetric Studies of Structure-Activity Relationships

AUTHOR(S): Strickland, Corey L.; Weber, Patricia C.; Windsor, William T.; Wu, Zhen; Le, Hung V.; Albanese, Margaret M.; Alvarez, Carmen S.; Cesarz, David; del Rosario, Joycelyn; Deskus, Jeffrey; Mallams, Alan K.; Njoroge, F. George; Piwinski, John J.; Remiszewski, Stacy; Rossman, Randall R.; Taveras, Arthur G.; Vibulbhan, Bancho; Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Ganguly, Ashit K.

CORPORATE SOURCE: Departments of Structural Chemistry and Chemical Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Journal of Medicinal Chemistry (1999), 42(12), 2125-2135

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 193275-84-2, SCH 66336 193275-85-3

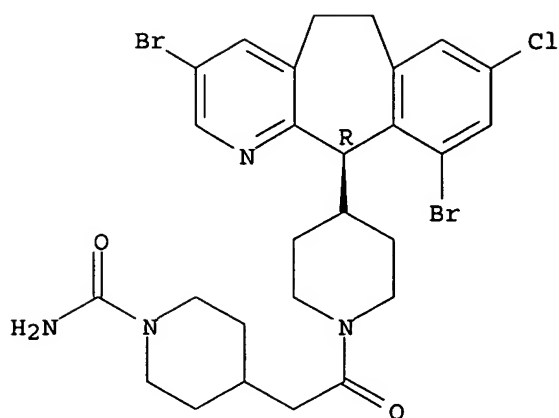
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(tricyclic farnesyl protein transferase inhibitors and crystallog. and calorimetric studies of structure-activity relationships)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

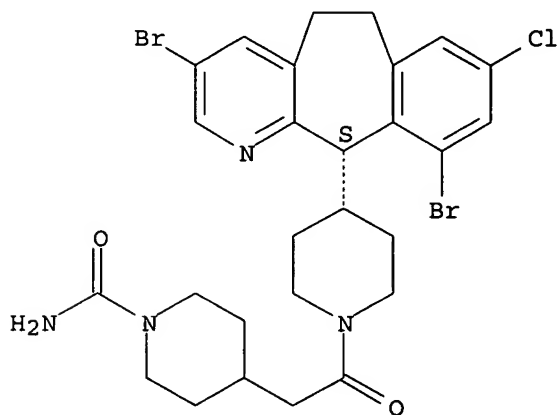
Absolute stereochemistry. Rotation (+).



RN 193275-85-3 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



AB Crystallog. and thermodyn. studies of farnesyl protein transferase (FPT) complexed with novel tricyclic inhibitors provide insights into the observed SAR for this unique class of nonpeptidic FPT inhibitors. The crystallog. structures reveal a binding pattern conserved across the mono-, di-, and trihalogen series. In the complexes, the tricycle spans the FPT active site cavity and interacts with both protein atoms and the isoprenoid portion of bound farnesyl diphosphate. An amide carbonyl, common to the tricyclic compds. described here, participates in a water-mediated hydrogen bond to the protein backbone. Ten high-resolution crystal structures of inhibitors complexed with FPT are reported. Included are crystallog. data for FPT complexed with SCH 66336, a compound currently undergoing clin. trials as an anticancer agent (SCH 66336, 4-[2-[4-(3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl)-1-piperidinyl]-2-oxoethyl]-1-piperidinecarboxamide). Thermodyn. binding parameters show favorable enthalpies of complex formation and small net entropic contributions as observed for 4-[2-[4-(3,10-dibromo-8-chloro-6,11-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-1-piperidinyl]-2-oxoethyl]pyridine N-oxide where $\Delta H^{\circ}_{\text{bind}} = -12.5$ kcal/mol and $T\Delta S^{\circ}_{\text{bind}} = -1.5$ kcal/mol.

REFERENCE COUNT:

41

THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:564267 HCAPLUS <<LOGINID::20060913>>

DOCUMENT NUMBER: 129:197984

TITLE: Combined tumor suppressor gene therapy and chemotherapy in the treatment of neoplasms

INVENTOR(S): Nielsen, Loretta; Horowitz, Jo Ann; Maneval, Daniel C.; Demers, G. William; Rybak, Mary Ellen; Resnick, Gene

PATENT ASSIGNEE(S): Canji, Inc., USA

SOURCE: PCT Int. Appl., 114 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9835554	A2	19980820	WO 1998-US3514	19980217
WO 9835554	A3	19981126		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
CA 2282683	AA	19980820	CA 1998-2282683	19980217
AU 9864380	A1	19980908	AU 1998-64380	19980217
AU 737621	B2	20010823		
EP 969720	A2	20000112	EP 1998-910038	19980217
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
NZ 337283	A	20010223	NZ 1998-337283	19980217
JP 2001511815	T2	20010814	JP 1998-536033	19980217
BR 9807418	A	20020122	BR 1998-7418	19980217
US 2003060434	A1	20030327	US 1999-311772	19990513
NO 9903943	A	19991015	NO 1999-3943	19990817
US 2003064949	A1	20030403	US 2002-86294	20020228
US 2004235736	A1	20041125	US 2004-824058	20040413
US 2005142112	A1	20050630	US 2004-823932	20040413
PRIORITY APPLN. INFO.:			US 1997-38065P	P 19970218
			US 1997-801285	A 19970218
			US 1997-801681	A 19970218
			US 1997-801755	A 19970218
			US 1997-801765	A 19970218
			US 1997-47834P	P 19970528
			US 1998-24932	B1 19980217
			WO 1998-US3514	W 19980217
			US 1999-311772	B3 19990513

IT 193275-84-2

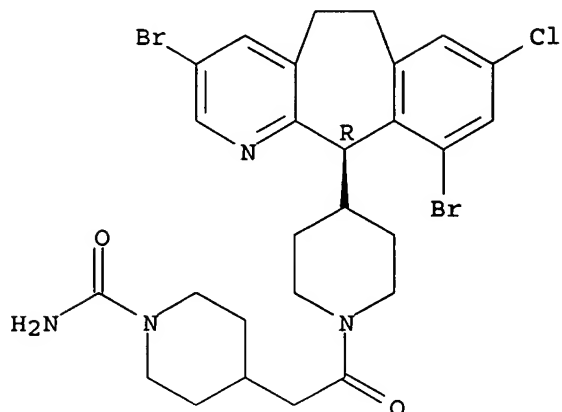
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tumor suppressor gene therapy-chemotherapy combination for treatment of neoplasms and hyperproliferative cells)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



AB In one embodiment, the invention provides methods of treating mammalian cancer or hyperproliferative cells, the method comprising contacting the cells with a tumor suppressor protein or tumor suppressor nucleic acid and also contacting the cells with at least one adjunctive anticancer agent. The invention also provides for a pharmacol. composition comprising a tumor suppressor protein or a tumor suppressor nucleic acid and at least one adjunctive anti-cancer agent, as well as a kit for the treatment of mammalian cancer or hyperproliferative cells.

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	167.82	178.76

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 FILE LAST UPDATED: 12 Sep 2006 (20060912/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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L11 252 L10

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3125 HYPOCALCEMIA
 7 HYPOCALCEMIAS
 3131 HYPOCALCEMIA
 (HYPOCALCEMIA OR HYPOCALCEMIAS)
 5273 HYPERCALCEMIA
 27 HYPERCALCEMIAS
 5280 HYPERCALCEMIA
 (HYPERCALCEMIA OR HYPERCALCEMIAS)
 4337 HYPERPARATHYROIDISM
 5 HYPERPARATHYROIDISMS
 4337 HYPERPARATHYROIDISM
 (HYPERPARATHYROIDISM OR HYPERPARATHYROIDISMS)
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 240606 "DISEASES"
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 1292203 "ANIMAL"
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 1627620 "ANIMAL"
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 28970 "DISEASE, ANIMAL"
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 68108 "ENDOCRINE"
 366 "ENDOCRINES"
 68250 "ENDOCRINE"
 ("ENDOCRINE" OR "ENDOCRINES")
 2319186 "SYSTEM"
 1270331 "SYSTEMS"
 3143835 "SYSTEM"

("SYSTEM" OR "SYSTEMS")
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 928 "PARATHYROIDS"
 21954 "PARATHYROID"
 ("PARATHYROID" OR "PARATHYROIDS")
 286645 "GLAND"
 69788 "GLANDS"
 313902 "GLAND"
 ("GLAND" OR "GLANDS")
 885305 "DISEASE"
 240606 "DISEASES"
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 ("DISEASE" OR "DISEASES")
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 36 "CALCIUMS"
 779786 "CALCIUM"
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 138025 METAST?
 2177 BON? METAST?
 (BON? (W) METAST?)
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 56 PTHS
 11557 PTH
 (PTH OR PTHS)
 16508 CALCITONIN
 853 CALCITONINS
 16821 CALCITONIN
 (CALCITONIN OR CALCITONINS)
 4051 GRANULOMATOUS
 2154 SARCOIDOSIS
 3438 CALCITRIOL
 4 CALCITRIOLS
 3439 CALCITRIOL
 (CALCITRIOL OR CALCITRIOLS)
 1921 HEMATOLOGIC
 21351 HEMATOL
 22241 HEMATOLOGIC
 (HEMATOLOGIC OR HEMATOL)
 15128 MALIGNANCY
 15132 MALIGNANCIES
 27999 MALIGNANCY
 (MALIGNANCY OR MALIGNANCIES)
 2922 HEMATOLOGIC MALIGNANCY
 (HEMATOLOGIC (W) MALIGNANCY)
 4952 LYMPHOPRO?

L12 34 L11 AND (HYPOCALCEMIA OR HYPERCALCEMIA OR (HYPERPARATHYROIDISM
 OR "DISEASE, ANIMAL") OR "ENDOCRINE SYSTEM, DISEASE" OR "PARATHY
 ROID GLAND, DISEASE" OR "CALCIUM" OR (BON? METAST?) OR PTH OR
 CALCITONIN OR GRANULOMATOUS OR SARCOIDOSIS OR CALCITRIOL OR (HEMA
 TOLOGIC MALIGNANCY) OR LYMPHOPRO?)

=> d l12 scan

L12 34 ANSWERS HCAPLUS COPYRIGHT 2006 ACS on STN
 IC ICM A61K031-59

INCL 514167000
 CC 1-6 (Pharmacology)
 Section cross-reference(s): 63
 TI Methods of using vitamin D compounds in the treatment of myelodysplastic syndromes
 ST vitamin D compd treatment myelodysplastic syndrome; calcitriol treatment myelodysplastic syndrome
 IT Glycerides, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (C8-10, MIGLYOL 812; vitamin D compds. in treatment of myelodysplastic syndromes)
 IT Suspensions
 (agent for making, as additive; vitamin D compds. in treatment of myelodysplastic syndromes)
 IT Thiols, biological studies
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (amino, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
 IT Antibodies and Immunoglobulins
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antilymphocyte globulins, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
 IT Antibodies and Immunoglobulins
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antithymocyte globulins, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
 IT Antifoaming agents
 Antioxidants
 Binders
 Buffers
 Chelating agents
 Coloring materials
 Fillers
 Flavoring materials
 Lubricants
 Odor and Odorous substances
 Opacifiers
 Plasticizers
 Preservatives
 Thickening agents
 (as additive; vitamin D compds. in treatment of myelodysplastic syndromes)
 IT Cytotoxic agents
 Immunomodulators
 (as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
 IT Cytokines
 Growth factors, animal
 Hemopoietins
 Interleukin 1
 Interleukin 11
 Interleukin 12
 Interleukin 2
 Interleukin 3
 Interleukin 6
 Interleukin 8
 Tocopherols
 Transcription factors
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (as addnl. active agent; vitamin D compds. in treatment of

myelodysplastic syndromes)

IT Drug delivery systems
(capsules; vitamin D compds. in treatment of myelodysplastic syndromes)

IT Gelatins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(capsules; vitamin D compds. in treatment of myelodysplastic syndromes)

IT Peptides, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(depsipeptides, as addnl. active agent; vitamin D compds. in treatment
of myelodysplastic syndromes)

IT Tackifiers
(detackifiers, as additive; vitamin D compds. in treatment of
myelodysplastic syndromes)

IT Signal transduction, biological
(inhibitors, as addnl. active agent; vitamin D compds. in treatment of
myelodysplastic syndromes)

IT Drug delivery systems
(injections, i.v.; vitamin D compds. in treatment of myelodysplastic
syndromes)

IT Viscosity
(modulators, as additive; vitamin D compds. in treatment of
myelodysplastic syndromes)

IT Stability
(of calcitriol capsules; vitamin D compds. in treatment of
myelodysplastic syndromes)

IT Solvates
Stereoisomers
(of vitamin D compds.; vitamin D compds. in treatment of
myelodysplastic syndromes)

IT Clathrates
Hydrates
Salts, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of vitamin D compds.; vitamin D compds. in treatment of
myelodysplastic syndromes)

IT Drug delivery systems
(prodrugs, of vitamin D compds.; vitamin D compds. in treatment of
myelodysplastic syndromes)

IT Drug targets
(related to MDS, agents binding to, as addnl. active agent; vitamin D
compds. in treatment of myelodysplastic syndromes)

IT Amines, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thiol, as addnl. active agent; vitamin D compds. in treatment of
myelodysplastic syndromes)

IT Combination chemotherapy
Human
Myelodysplastic syndromes
(vitamin D compds. in treatment of myelodysplastic syndromes)

IT Interferons
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α , as addnl. active agent; vitamin D compds. in treatment of
myelodysplastic syndromes)

IT 127464-60-2, VEGF
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(anti-VEGF, as addnl. active agent; vitamin D compds. in treatment of
myelodysplastic syndromes)

IT 50-02-2, Dexamethasone 50-35-1, Thalidomide 53-03-2, Prednisone
147-94-4, Cytarabine 148-82-3, Melphalan 302-79-4, Retinoic acid
320-67-2, 5-Azacytidine 863-61-6, Menatetrenone 1327-53-3, Arsenic

trioxide 1406-18-4D, Vitamin E, derivs. 2353-33-5, Decitabine
 4346-18-3, Phenyl butyrate 4759-48-2 6493-05-6, Pentoxifylline
 9002-96-4, Vitamin E TPGS 9014-42-0, Thrombopoietin 11096-26-7, EPO
 11103-57-4D, Vitamin A, derivs. 12001-79-5D, Vitamin K, derivs.
 20537-88-6, Amifostine 20830-81-3, Daunorubicin 21679-14-1,
 Fludarabine 33419-42-0, Etoposide 58957-92-9, Idarubicin 59865-13-3,
 Cyclosporin A 65271-80-9, Mitoxantrone 83869-56-1, GM-CSF
 123948-87-8, Topotecan 143011-72-7, Granulocyte-colony stimulating
 factor 185243-69-0, TNFR:Fc 192185-72-1, ZARNESTRA 193275-84-2
 , SARASAR 204005-46-9, SU5416 212142-18-2 220578-59-6, Gemtuzumab
 ozogamicin 252916-29-3, SU6668
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (as addnl. active agent; vitamin D compds. in treatment of
 myelodysplastic syndromes)
 IT 32222-06-3, Calcitriol
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study);
 USES (Uses)
 (as vitamin D compound; vitamin D compds. in treatment of myelodysplastic
 syndromes)
 IT 7440-38-2, Arsenic, biological studies
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (compound containing, as addnl. active agent; vitamin D compds. in treatment
 of myelodysplastic syndromes)
 IT 1406-16-2D, Vitamin D, compds.
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (vitamin D compds. in treatment of myelodysplastic syndromes)
 IT 128-37-0, Butylated hydroxytoluene, biological studies 25013-16-5,
 Butylated hydroxyanisole 121548-04-7, Gelucire 44/14
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (vitamin D compds. in treatment of myelodysplastic syndromes)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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 FILE 'HOME' ENTERED AT 19:55:41 ON 13 SEP 2006
 FILE 'REGISTRY' ENTERED AT 20:03:37 ON 13 SEP 2006
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 FILE 'HCAPLUS' ENTERED AT 20:04:03 ON 13 SEP 2006
 FILE 'REGISTRY' ENTERED AT 20:04:13 ON 13 SEP 2006
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 L5 50 S L4 SSS SAM
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L8 STRUCTURE UPLOADED

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L10 1034 S L8 SSS FULL

FILE 'HCAPLUS' ENTERED AT 20:15:09 ON 13 SEP 2006

L11 252 S L10

E HYPOCALCEMIA+ALL/CT

E HYPERCALCEMIA+ALL/CT

E HYPERPARATHYROIDISM+ALL/CT

L12 34 S L11 AND (HYPOCALCEMIA OR HYPERCALCEMIA OR (HYPERPARATHYROIDIS

=> d l12 ibib abs hitstr

L12 ANSWER 1 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:608613 HCAPLUS

DOCUMENT NUMBER: 145:83394

TITLE: Piperazine derivatives as farnesyl protein transferase inhibitors and their preparation, pharmaceutical compositions and methods for treating proliferative diseases

INVENTOR(S): Mallams, Alan K.

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 337 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006065794	A1	20060622	WO 2005-US45019	20051212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2004-636451P P 20041214

OTHER SOURCE(S): MARPAT 145:83394

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed are compds. of the formula I and their pharmaceutically acceptable salts. Compds. of formula I wherein dotted lines is optional double bonds; a, b, c and d is CR1; one of a, b, c and d are N or N+O-; R1, R3 and R4 are independently is H, halo, CF3, OH and derivs., CHO, acyl, S(O)tH and derivs., NH2 and derivs., NO2, CO2H and derivs., CN, etc.; t is 0, 1 or 2; R4R4 taken together represent a (un)saturated C5-7 fused ring to the benzene ring; R5, R6 and R7 are independently H, CF3, CHO, acyl, (un)substituted alkyl, or (un)substituted aryl; X is N, CH, or C; A and B are independently absent, Hm alkyl, aryl, aralkyl, OH and derivs., OCO2H and derivs., OCHO, and O-acyl, etc.; R8 when X is CH or C is H,

COYR12 or SO2R13; R8 when X is N is H, COTR12, SO2R13 or a tricyclic ring system, etc; R9 is halo, (un)substituted alkyl, trifluoroalkyl, HO, alkyloxy, amino or acylamino; R11 is H, alkyl, or arylalkyl; Y is (un)substituted methylene or NH; R12 is (un)substituted (hetero)(cyclo)alkyl, or (un)substituted (hetero)aryl(alkyl); R13 is (un)substituted (cyclo)alkyl or (un)substituted (aryl)alkyl; R16 is unsubstituted imidazole; m is 0 to 4; n is 1, 2, 3 or 4; and their pharmaceutically acceptable salts are claimed. Also disclosed are uses of the compds. of formula I for the manufacture of a medicament for treating cancer and for inhibiting farnesyl protein transferase. Example compound II was prepared by amidation of compound III with 1-(3-aminobenzyl)imidazole to give racemic compound II was separated by chiral HPLC to give the enantiomerically enriched compound II. All the invention compds. were evaluated for their farnesyl protein transferase inhibitory activity. From the assay, it was determined that most of the tested compds. exhibited good IC50 values in the range of < 0.05 nM to about 200 nM.

IT 892392-87-9P 892392-96-0P 892393-02-1P

892393-03-2P

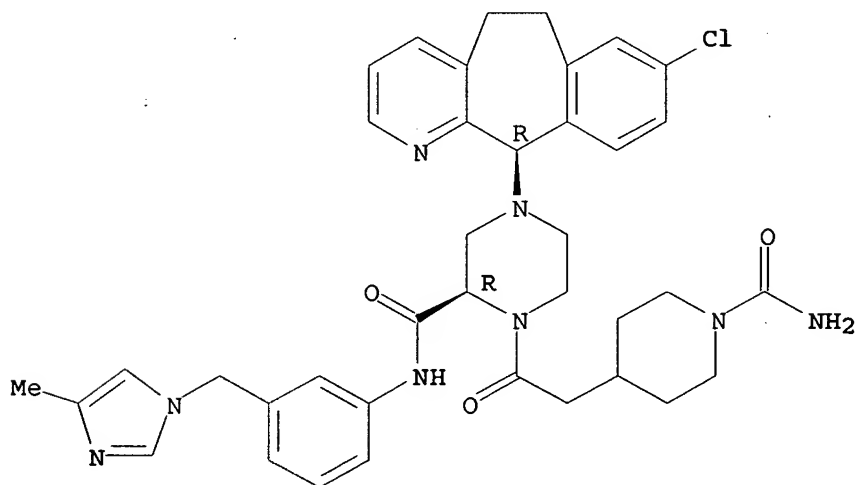
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of piperazine derivs. as farnesyl protein transferase inhibitors useful in treatment of cancer and other proliferative diseases)

RN 892392-87-9 HCAPLUS

CN 2-Piperazinecarboxamide, 1-[[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-4-[(11R)-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-N-[3-[(4-methyl-1H-imidazol-1-yl)methyl]phenyl]-, (2R)- (9CI) (CA INDEX NAME)

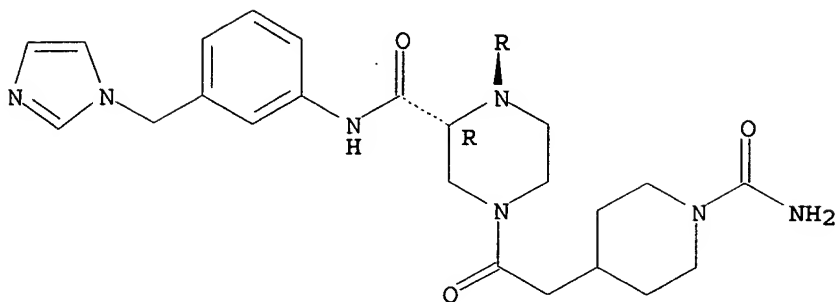
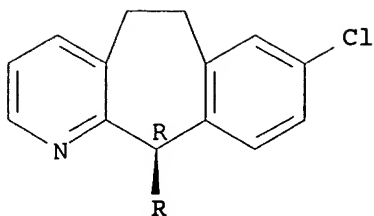
Absolute stereochemistry. Rotation (+).



RN 892392-96-0 HCAPLUS

CN 2-Piperazinecarboxamide, 4-[[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-1-[(11R)-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-N-[3-(1H-imidazol-1-ylmethyl)phenyl]-, (2R)- (9CI) (CA INDEX NAME)

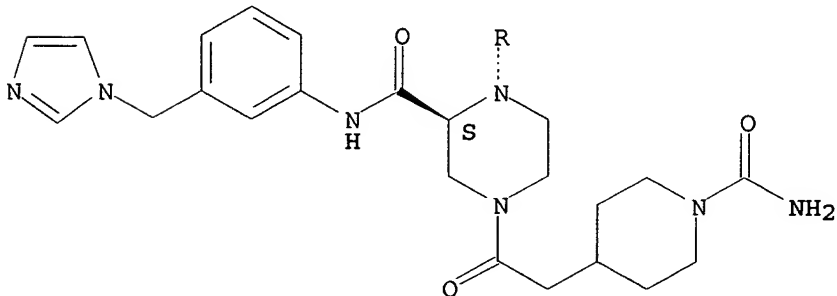
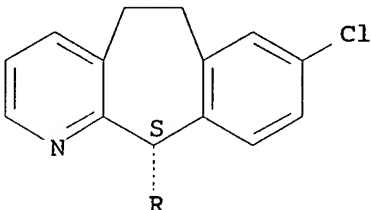
Absolute stereochemistry. Rotation (+).



RN 892393-02-1 HCAPLUS

CN 2-Piperazinecarboxamide, 4-[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-1-[(11S)-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-N-[3-(1H-imidazol-1-ylmethyl)phenyl]-, (2S)- (9CI) (CA INDEX NAME)

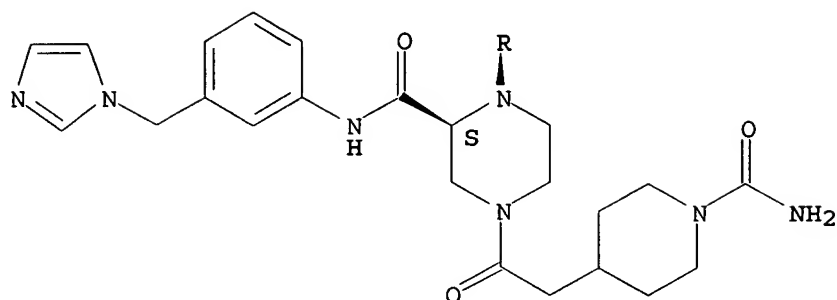
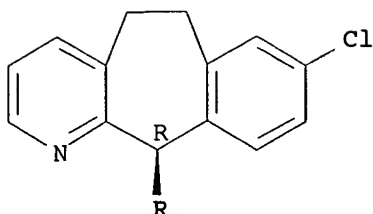
Absolute stereochemistry. Rotation (-).



RN 892393-03-2 HCAPLUS

CN 2-Piperazinecarboxamide, 4-[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-1-[(11R)-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-N-[3-(1H-imidazol-1-ylmethyl)phenyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l12 ibib abs hitstr 2-32

L12 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:463553 HCAPLUS

DOCUMENT NUMBER: 144:488677

TITLE: Preparation of novel imidazopyrazines as cyclin dependent kinase inhibitors

INVENTOR(S): Guzi, Timothy J.; Paruch, Kamil; Dwyer, Michael P.; Zhao, Lianyun; Curran, Patrick J.; Belanger, David B.; Hamann, Blake; Reddy, Panduranga A.; Siddiqui, M. Arshad

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 161 pp., Cont.-in-part of U.S. Ser. No. 47,524.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

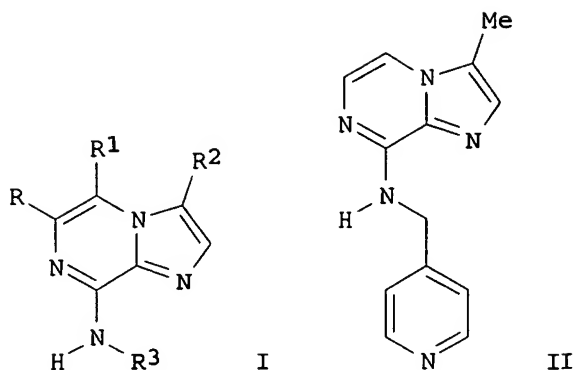
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006106023	A1	20060518	US 2005-272392	20051110
US 2004063715	A1	20040401	US 2003-665005	20030919
US 6919341	B2	20050719		
US 2005130980	A1	20050616	US 2005-47524	20050131
PRIORITY APPLN. INFO.:			US 2002-412997P	P 20020923
			US 2003-665005	A3 20030919
			US 2005-47524	A2 20050131

OTHER SOURCE(S): MARPAT 144:488677

GI

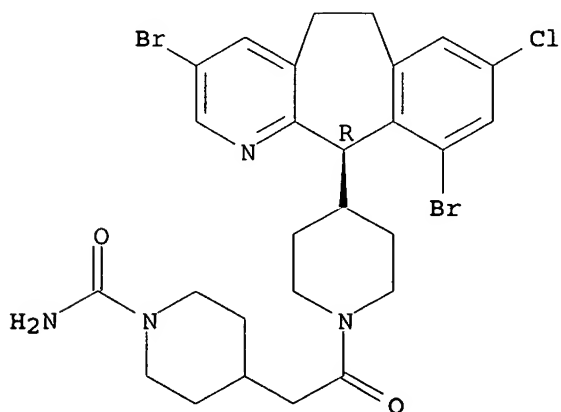


AB In its many embodiments, the present invention provides a novel class of imidazo[1,2-a]pyrazine compds. of formula I [R = H, halo, (un)substituted-aryl, -heteroaryl, -cycloalkyl, etc.; R¹ = H, halo or alkyl; R² = halo, (un)substituted-alkyl, -aryl, -arylalkyl, etc.; R³ = H, (un)substituted-aryl, -heteroaryl, -heterocyclyl, etc.] as inhibitors of cyclin dependent kinases, methods of preparing such compds., pharmaceutical compns. containing one or more such compds., methods of preparing pharmaceutical formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the CDKs using such compds. or pharmaceutical compns. Thus, e.g., II was prepared by condensation of 8-chloro-3-methylimidazo[1,2-a]pyrazine with 4-(aminomethyl)pyridine. I possessed excellent CDK inhibitory properties, e.g., II demonstrated an IC₅₀ value of 22.5 μ M.

IT 193275-84-2, SCH 66336
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation of novel imidazopyrazines as cyclin dependent kinase inhibitors useful in treatment and prevention of various diseases)

RN 193275-84-2 HCAPLUS
 CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2006:366977 HCAPLUS
 DOCUMENT NUMBER: 144:412498
 TITLE: Preparation of substituted N-aryl-1H-pyrazolo[3,4-b]quinolin-4-amines and analogs as activators of

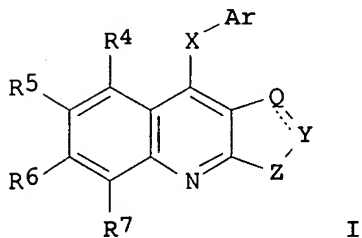
caspace and inducers of apoptosis
 INVENTOR(S): Zhang, Han-Zhong; Cai, Sui Xiong; Drewe, John A.
 PATENT ASSIGNEE(S): Cytovia, Inc., USA
 SOURCE: PCT Int. Appl., 79 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006041900	A2	20060420	WO 2005-US35793	20051006
WO 2006041900	A3	20060713		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-616539P P 20041007
 OTHER SOURCE(S): MARPAT 144:412498
 GI



AB The title compds. I [X = O, NR3, S, SO, SO2; Ar = (un)substituted aryl, heteroaryl, carbocyclyl, etc.; Q = CR2, CR12R13; Y = N, CR10R11; Z = NR1, CR8R9; R1, R3 = H, (un)substituted alkyl; R2, R4-R13 = H, halo, aryl, etc.] which are activators of caspases and inducers of apoptosis and therefore can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs (biol. data given), were prepared E.g., a multi-step synthesis of 1,3-dimethyl-N-[4-(methoxycarbonyl)phenyl]-1H-pyrazolo[3,4-b]quinolin-4-amine, starting from anthranilic acid and 4-methyleneoxetan-2-one, was given. Pharmaceutical composition comprising the compound I alone or in combination with other therapeutic agents are disclosed.

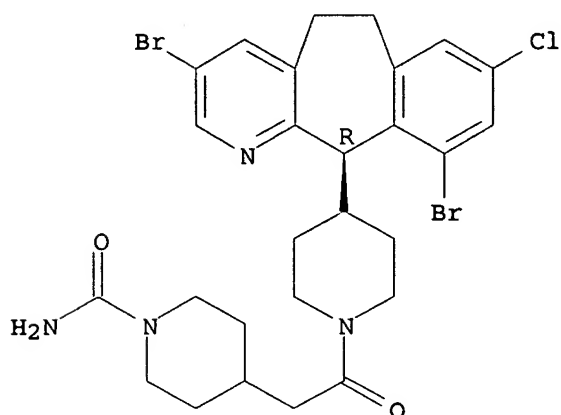
IT 193275-84-2, SCH66336
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation of substituted N-aryl-1H-pyrazolo[3,4-b]quinolin-4-amines and analogs as activators of caspases and inducers of apoptosis)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-

(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:317333 HCAPLUS

DOCUMENT NUMBER: 144:363075

TITLE: Use of inhibitors of 24-hydroxylase in combination with other agents for the treatment of cancer

INVENTOR(S): Polvino, William J.

PATENT ASSIGNEE(S): Sapphire Therapeutics, Inc., USA

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006036892	A2	20060406	WO 2005-US34410	20050923
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

US 2006078494 A1 20060413 US 2005-234552 20050923

PRIORITY APPLN. INFO.: US 2004-612712P P 20040924

OTHER SOURCE(S): MARPAT 144:363075

AB The invention discloses a method for treating cancer in a subject. The method comprises administering to a subject suffering from cancer a therapeutically effective amount of a 24-hydroxylase inhibitor in combination with a second amount of a suitable cancer therapeutic. The 24-hydroxylase inhibitor can be coadministered with a chemotherapeutic agent, such as an antitumor antibiotic (e.g., mitoxantrone or bleomycin), an alkylating agent (e.g., estramustine or melphalan), a plant alkaloid (e.g., taxanes such as paclitaxel or docetaxel or viva alkaloids such as vincristine or vinblastine) or a combination thereof. In addnl. therapy, the 24-hydroxylase inhibitor can be coadministered as an adjuvant to

radiation therapy, such as an external beam irradiation or a radioisotope therapy, such as radiopharmaceutical therapy. Further, the 24-hydroxylase inhibitor can be coadministered as part of a combination therapy that includes hormonal ablation.

IT 193275-84-2, Lonafarnib

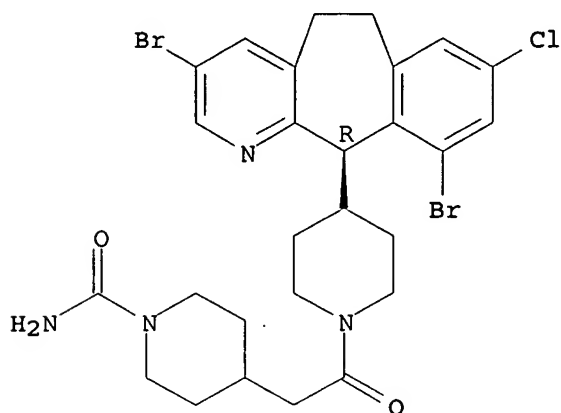
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(vitamin D 24-hydroxylase inhibitor combination with other agent for treatment of cancer)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:98364 HCAPLUS

DOCUMENT NUMBER: 144:460150

TITLE: Farnesyl transferase inhibitors

AUTHOR(S): Basso, Andrea D.; Kirschmeier, Paul; Bishop, W. Robert

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Journal of Lipid Research (2006), 47(1), 15-31

CODEN: JLPRAW; ISSN: 0022-2275

PUBLISHER: American Society for Biochemistry and Molecular Biology, Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Some proteins undergo posttranslational modification by the addition of an isoprenyl lipid (farnesyl- or geranylgeranyl-isoprenoid) to a cysteine residue proximal to the C terminus. Protein isoprenylation promotes membrane association and contributes to protein-protein interactions. Farnesylated proteins include small GTPases, tyrosine phosphatases, nuclear lamina, cochaperones, and centromere-associated proteins. Prenylation is required for the transforming activity of Ras. Because of the high frequency of Ras mutations in cancer, farnesyl transferase inhibitors (FTIs) were investigated as a means to antagonize Ras function. Evaluation of FTIs led to the finding that both K- and N-Ras are alternatively modified by geranylgeranyl prenyltransferase-1 in FTI-treated cells. Geranylgeranylated forms of Ras retain the ability to associate with the plasma membrane and activate substrates. Despite this, FTIs are effective at inhibiting the growth of human tumor cells in vitro, suggesting that activity is dependent on blocking the farnesylation of other proteins. FTIs also inhibit the in vivo growth of human tumor xenografts and sensitize these models to chemotherapeutics, most notably

taxanes. Several FTIs have entered clin. trials for various cancer indications. In some clin. settings, primarily hematol. malignancies, FTIs have displayed evidence of single-agent activity. Clin. studies in progress are exploring the antitumor activity of FTIs as single agents and in combination. This review will summarize the basic biol. of FTIs, their antitumor activity in preclin. models, and the current status of clin. studies with these agents.

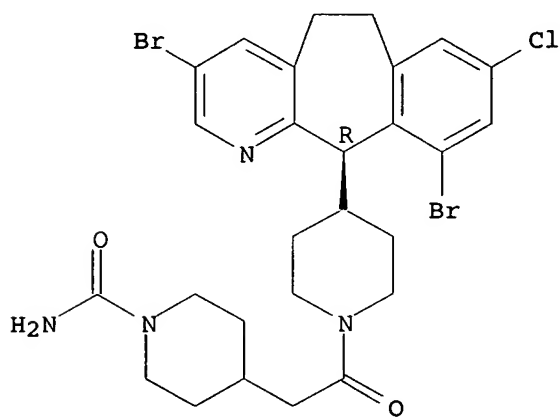
IT 193275-84-2, Lonafarnib

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (farnesyl transferase inhibitors)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 220 THERE ARE 220 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L12 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:40315 HCAPLUS

DOCUMENT NUMBER: 144:460119

TITLE: Farnesyltransferase inhibitors in myelodysplastic syndrome

AUTHOR(S): Feldman, E. J.

CORPORATE SOURCE: Weill Medical College, Cornell University, New York, NY, 10021, USA

SOURCE: Current Hematology Reports (2005), 4(3), 186-190
CODEN: CHRUEI; ISSN: 1540-3408

PUBLISHER: Current Science Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. The farnesyltransferase inhibitors (FTIs) are in active clin. development in a variety of human malignancies. The most promising activity to date has been demonstrated in patients with hematol. malignancies, in particular acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). In patients with MDS, two non-peptido-mimetic agents, tipifarnib (Zarnestra, Johnson & Johnson, New Brunswick, NJ) and lonafarnib (Sarasar, Schering-Plough, Kenilworth, NJ) have been the most extensively studied. In both phase I and phase II trials, tipifarnib has demonstrated significant efficacy with overall response rates of 30%, with complete remissions in about 15%. Dose-limiting side effects have been primarily myelosuppression, although fatigue, neurotoxicity, and occasional renal dysfunction have required

dose redns. Lonafarnib in patients with MDS has also resulted in clin. responses in approx. 30%, including significant improvements in platelet counts. Lonafarnib has been associated with primarily diarrhea and other gastrointestinal toxicity, anorexia, and nausea, which has limited its efficacy. Clin. response correlation with documentation of inhibition of farnesyltransferase and/or evidence of decreased farnesylation of downstream protein targets has not been demonstrated with either agent. In addition, the presence of an activating Ras mutation has not predicted response to therapy with FTIs in MDS and AML. Despite this, significant clin. efficacy of the FTIs in MDS, on par with that of currently available chemotherapeutic agents, has been observed, leading to further development of this new class of drugs in MDS and AML.

IT 193275-84-2, Sarasar

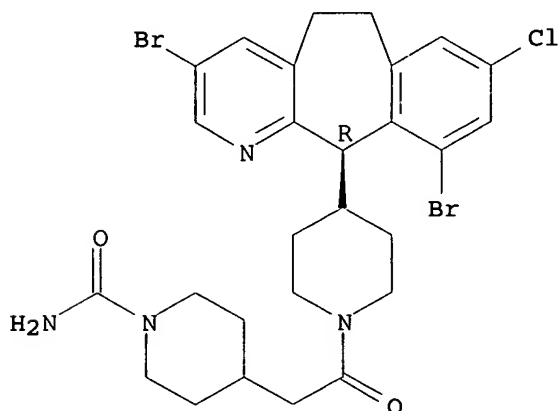
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phase I and II trial of FTI lonafarnib improved platelet count and showed clin. response with limited efficacy and was associated with primarily diarrhea, gastrointestinal toxicity, anorexia and nausea in patient with MDS)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1290072 HCAPLUS

DOCUMENT NUMBER: 144:46998

TITLE: The X-ray crystal structure of BRCA1 tandem BRCT repeat and BACH1 phosphopeptide complex and methods and compositions for antitumor drug design

INVENTOR(S): Yaffe, Michael B.; Clapperton, Julie A.; Manke, Isaac A.; Lowery, Drew M.; Ho, Timmy; Haire, Lesley F.; Smerdon, Stephen J.

PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA

SOURCE: PCT Int. Appl., 360 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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 WO 2005115454 A2 20051208 WO 2005-US15981 20050509
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
 LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
 NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
 SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
 ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2004-569131P

P 20040507

AB The present invention relates to compds. (e.g., peptidomimetics and non-peptides) that treat, prevent or stabilize cellular proliferative disorders and methods of treating, preventing, or stabilizing such disorders. The invention also provides three-dimensional structures of a BRCT domain-BACH1 phosphopeptide complex.

IT 193275-84-2, Sarasar

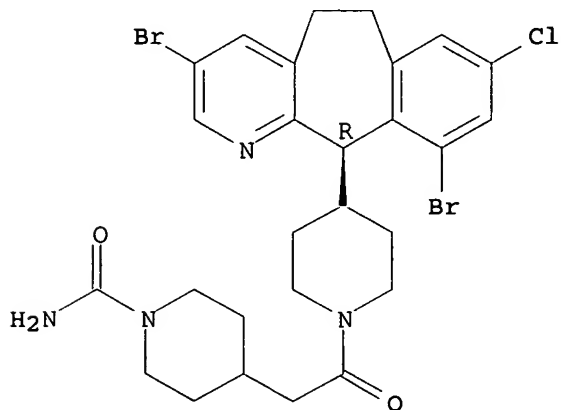
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(X-ray crystal structure of BRCA1 tandem BRCT repeat and BACH1 phosphopeptide complex and methods and compns. for antitumor drug design)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1239173 HCAPLUS

DOCUMENT NUMBER: 143:477963

TITLE: Preparation of pyrazolyl urea derivatives as TrkA kinase inhibitors useful in the treatment of cancer

INVENTOR(S): Lee, Wendy; Ladouceur, Gaetan; Dumas, Jacques; Smith, Roger; Ying, Shihong; Wang, Gan; Chen, Zhi; Liu, Qingjie; Mokdad, Holia Hatoum

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 215 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005110994	A2	20051124	WO 2005-US15106	20050502
WO 2005110994	A3	20060202		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-566445P P 20040430

OTHER SOURCE(S): MARPAT 143:477963

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

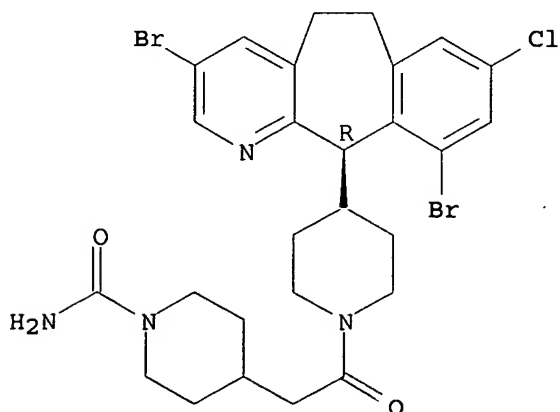
AB Title compds. I [R1-2 = H, alkyl, halo; A = Ph, pyridine, pyrimidine; B = phenylene, naphthylene; L = O, S, CH₂; M = Ph, pyridine, pyrimidine; n = 0-1; X = O, SO₂, etc.; Y = alkoxy, oxycarbonyl, amino, etc.] are prepared For instance, II is prepared from 4-[3-tert-butyl-5-[N'-[4-(pyridin-4-yloxy)phenyl]ureido]pyrazol-1-yl]benzoic acid Me ester (preparation given) and 2-(pyrrolidin-1-yl)ethylamine (DCE, AlMe₃, 80°, 16 h). Compds. of the invention show significant inhibition of TrkA kinase (IC₅₀ < 1 μM). I are useful for the treatment of cancer.

IT 193275-84-2, Lonafarnib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substituted pyrazolylurea derivs. useful for cancer treatment)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:904338 HCAPLUS

DOCUMENT NUMBER: 143:248417

TITLE: Preparation of pyrazolotriazines as kinase inhibitors for treating cancer and other diseases associated with a kinase

INVENTOR(S): Guzi, Timothy J.; Paruch, Kamil

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 45 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

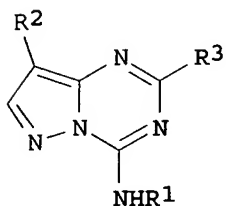
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005187219	A1	20050825	US 2005-64044	20050223
US 7038045	B2	20060502		
WO 2005082908	A1	20050909	WO 2005-US5614	20050223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006122389	A1	20060608	US 2006-335383	20060119
PRIORITY APPLN. INFO.:			US 2004-547685P	P 20040225
			US 2005-64044	A3 20050223

OTHER SOURCE(S): MARPAT 143:248417

GI



AB In its many embodiments, the present invention provides a novel class of pyrazolo[1,5-a]triazine compds. (I, variables defined below) as inhibitors of kinases such as, for example, cyclin dependent kinases, methods of preparing such compds., pharmaceutical compns. containing one or more such compds., methods of preparing pharmaceutical formulations comprising one or more such compds., and methods of treatment, prevention, inhibition, or amelioration of one or more diseases associated with the kinases using such compds. or pharmaceutical compns. For I, R1 is H, optionally substituted alkyl, aryl, heteroaryl, heteroarylalkyl, arylalkyl, NR6R7, cycloalkyl and cycloalkylalkyl; R2 is alkyl, cycloalkyl, alkenyl, alkynyl, trifluoromethyl, OR7, SR7, hydroxyalkyl, haloalkyl, aryl, heteroaryl, halo, CN, formyl, nitro, alkylcarbonyl, aralkylcarbonyl,

heteroaralkylcarbonyl, or alkylene-N(R8R9) [where R8 and R9 represent H or alkyl, or R8 and R9 taken together with the nitrogen in -N(R8R9) form a five- to seven-membered heterocycle]; R3 is -NR4R5, substituted heterocycle, H, alkyl, alkylthio, aralkylthio, alkylsulfinyl, or aralkylsulfinyl; R4 is optionally substituted alkyl, cycloalkyl or heterocyclyl; R5 is H, alkyl, aryl, heteroaryl, arylalkyl, cycloalkyl, heterocyclyl, acyl or heteroarylalkyl; R6 is H, alkyl or aryl; R7 is H or alkyl.

IT 193275-84-2, SCH66336

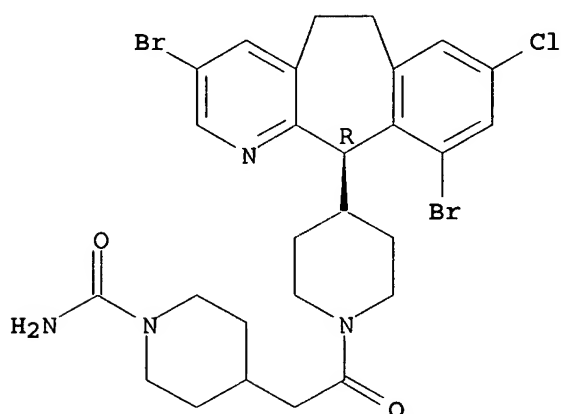
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of pyrazolotriazines as kinase inhibitors for treating cancer and other diseases associated with kinase in combination with other anticancer agents)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:700420 HCAPLUS

DOCUMENT NUMBER: 143:259750

TITLE: Characterization of a human carcinoma cell line selected for resistance to the farnesyl transferase inhibitor 4-(2-(4-(8-chloro-3,10-dibromo-6,11-dihydro-5H-benzo-(5,6)-cyclohepta(1,2-b)-pyridin-11(R)-yl)-1-piperidinyl)-2-oxo-ethyl)-1-piperidinecarboxamide (SCH66336)

AUTHOR(S): Bruzek, Laura M.; Poynter, Jenny N.; Kaufmann, Scott H.; Adjei, Alex A.

CORPORATE SOURCE: Department of Oncology, Mayo Clinic, Rochester, MN, USA

SOURCE: Molecular Pharmacology (2005), 68(2), 477-486
CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Farnesyl protein transferase inhibitors (FTIs) have demonstrated clin. activity in certain solid tumors and hematol. malignancies. Little is known about mechanisms of resistance to these agents. To provide a basis for better understanding FTI resistance,

the colorectal carcinoma cell line HCT 116 was selected by stepwise exposure to increasing 4-(2-(4-(8-chloro-3,10-dibromo-6,11-dihydro-5H-benzo(5,6)-cyclohepta(1,2-b)-pyridin-11(R)-yl)-1-piperidinyl)-2-oxoethyl)-1-piperidinecarboxamide (SCH66336) concns. The resulting line, HCT 116R, was 100-fold resistant to SCH66336 and other FTIs, including Me {N-[2-phenyl-4-N(2(R)-amino-3-mercaptopropylamino) benzoyl]}-methionate (FTI-277), but was less than 2-fold resistant to the standard agents gemcitabine, cisplatin, and paclitaxel. Accumulation of the unfarnesylated forms of prelamin A and HDJ-2, two substrates that reflect farnesyl transferase inhibition, was similar in FTI-treated parental and HCT 116R cells, indicating that alterations in drug uptake or inhibition of farnesyl protein transferase is not the mechanism of resistance. Changes in signal-transduction pathways that might account for this resistance were examined by immunoblotting and confirmed pharmacol. There was no difference in activation of the mitogen-activated protein kinase kinase (MEK)/extracellular signal-regulated kinase pathway or sensitivity to the MEK1/2 inhibitor 2'-amino-3'-methoxyflavone (PD98059) in HCT 116R cells. In contrast, increased phosphorylation of the mol. target of rapamycin (mTOR) and its downstream target p70 S6 kinase and increased levels of Akt1 and Akt2 were demonstrated in HCT 116R cells. Further expts. demonstrated that the mTOR inhibitor rapamycin selectively sensitized HCT 116R cells to SCH66336 but not to gemcitabine, cisplatin, or paclitaxel. These findings provide evidence that alterations in the phosphatidylinositol-3 kinase/Akt pathway can contribute to FTI resistance and suggest a potential strategy for overcoming this resistance.

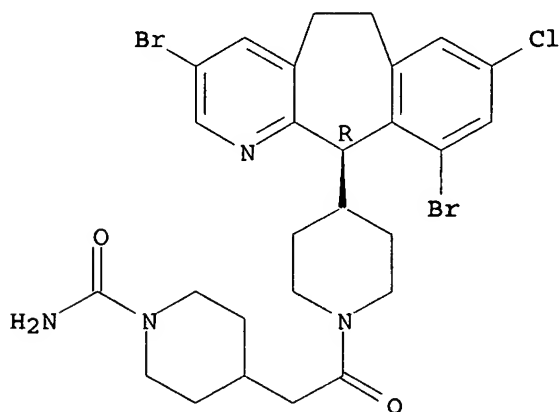
IT 193275-84-2, SCH66336

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of a human carcinoma cell line selected for resistance to the farnesyl transferase inhibitor SCH66336)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:588556 HCAPLUS

DOCUMENT NUMBER: 143:115395

TITLE: Preparation of derivatives of gambogic acid and analogs as activators of caspases and inducers of apoptosis

INVENTOR(S): Cai, Sui Xiong; Jiang, Songchun; Zhang, Han-Zhong

PATENT ASSIGNEE(S): Cytovia, Inc., USA
 SOURCE: PCT Int. Appl., 51 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005060663	A2	20050707	WO 2004-US42292	20041217
WO 2005060663	A3	20051222		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-530256P P 20031218
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

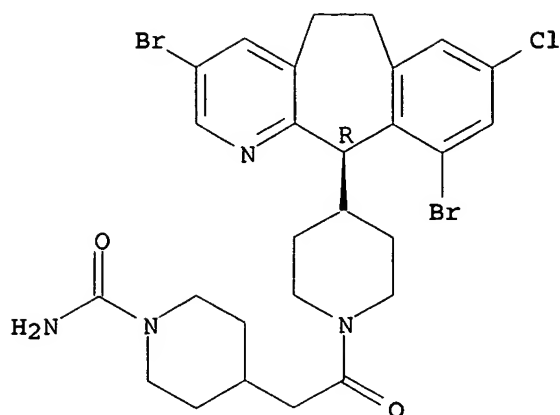
AB The present invention is directed to novel derivs. of gambogic acid (I) and analogs thereof. Thus, 2-(Dimethylamino)ethyl gambogate (II) was prepared from I via esterification with ClCH₂CH₂NMe₂·HCl in the presence of KI and Cs₂CO₄. The present invention also relates to the discovery that novel derivs. of gambogic acid are activators of caspases and inducers of apoptosis. Therefore, the activators of caspases and inducers of apoptosis of this invention can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs. The bioactivity of II was determined [caspase cascade activation EC₅₀ = 676 nM vs. T-47D and EC₅₀ = 1041 nM vs. DLD breast cancer cells; cell proliferation inhibition GI₅₀ = 187 nM (vs. T-47D), GI₅₀ = 173 nM (vs. DLD), GI₅₀ = 101 nM (vs. MX-1), GI₅₀ = 180 nM (vs. SW620), GI₅₀ = 184 nM (vs. H1299), GI₅₀ = 440 nM (vs. HEK293T), GI₅₀ = 192 nM (vs. HEK293H)].

IT 193275-84-2, SCH66336
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (combination chemotherapy co-agent; preparation of derivs. of gambogic acid and analogs as activators of caspases and inducers of apoptosis)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:409543 HCAPLUS

DOCUMENT NUMBER: 142:457053

TITLE: Human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy

INVENTOR(S): Lacasse, Eric; McManus, Daniel

PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.

SOURCE: PCT Int. Appl., 112 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042558	A1	20050512	WO 2004-CA1902	20041029
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2005148535	A1	20050707	US 2004-975974	20041028
CA 2542904	AA	20050512	CA 2004-2542904	20041029
EP 1682565	A1	20060726	EP 2004-789809	20041029

R: DE, FR, GB

PRIORITY APPLN. INFO.:

US 2003-516192P P 20031030

WO 2004-CA1902 W 20041029

AB The invention provides nucleobase oligomers and oligonucleotide duplexes that inhibit expression of an IAP (inhibitor of apoptosis protein), and methods for using them to induce apoptosis in a cell. Specifically, the invention provides nucleic acid sequences for siRNAs and shRNAs that target human XIAP, HIAP-1 or HIAP-2 genes. The nucleobase oligomers and oligomer complexes of the present invention may also be used to form pharmaceutical compns. The invention also features methods for enhancing apoptosis in a cell by administering a nucleobase oligomer or oligomer complex of the invention in combination with a chemotherapeutic or chemosensitizing agent. RNAi sequences and vectors producing shRNA (short

hairpin RNA) were transfected into HeLa cells and evaluated for their effect on XIAP, cIAP-1, or cIAP-2 protein levels. XIAP protein could also be reduced by RNAi clones in transfected breast cancer cell line MDA-MB-231. In addition, cell survival was reduced in XIAP RNAi transfected breast cancer cell line after the transfected cells were treated with TRAIL (tumor necrosis factor-related apoptosis inducing ligand).

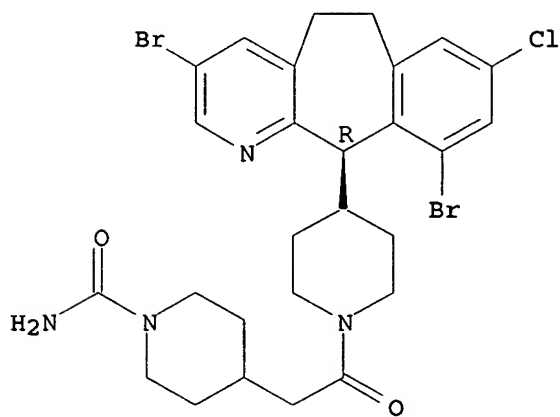
IT 193275-84-2, Lonafarnib

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:409357 HCAPLUS

DOCUMENT NUMBER: 142:457052

TITLE: Sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with a chemotherapeutic agent

INVENTOR(S): Lacasse, Eric; McManus, Daniel; Durkin, Jon P.

PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.

SOURCE: PCT Int. Appl., 285 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042030	A1	20050512	WO 2004-CA1900	20041029
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,			

SN, TD, TG
 US 2005119217 A1 20050602 US 2004-975790 20041028
 AU 2004284855 A1 20050512 AU 2004-284855 20041029
 CA 2542884 AA 20050512 CA 2004-2542884 20041029
 EP 1691842 A1 20060823 EP 2004-789807 20041029
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
 PRIORITY APPLN. INFO.: US 2003-516263P P 20031030
 WO 2004-CA1900 W 20041029

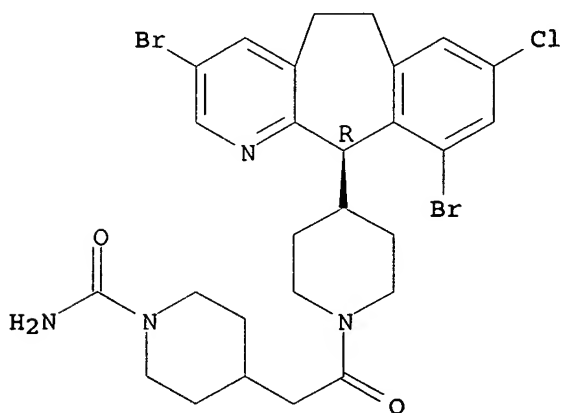
AB The invention claims the use of an antisense oligomer to human XIAP, IAP-1 or IAP-2 genes and a chemotherapeutic agent, and compns. and kits thereof, for the treatment of proliferative diseases. The invention further claims sequences for nucleobase oligomers that are antisense IAP (inhibitor of apoptosis protein) oligomers. The antisense IAP nucleobase oligomers specifically hybridize with polynucleotides encoding an IAP and reduce the amount of an IAP protein produced in a cell. Thus by reducing the IAP protein, the invention provides methods for inducing cancer cells to undergo apoptosis and for overriding anti-apoptotic signals in cancer cells. As an example of the invention, mice with s.c. H460 human lung carcinoma xenografts were injected intratumorally with XIAP antisense mixed-base 2'-O-Me RNA oligonucleotides (C5 and/or G4) and the drug vinorelbine. At the end of the 24 d treatment period, the mean relative tumor growth was reduced .apprx.70% in treated mice. The inhibition of tumor growth was correlated with down-regulation of human XIAP protein expression and an increased number of dead cells. The mice did not show any signs of cytotoxicity such as body weight loss.

IT 193275-84-2, Lonafarnib
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (sequences of antisense IAP (inhibitor of apoptosis protein) oligomers and their use for treatment of proliferative diseases with chemotherapeutic agent)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 14 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:409226 HCAPLUS

DOCUMENT NUMBER: 142:441858

TITLE: Methods of using vitamin D compounds in the treatment of myelodysplastic syndromes

INVENTOR(S): Whitehouse, Martha J.; Curd, John G.

PATENT ASSIGNEE(S): Novacea, Inc., USA
 SOURCE: U.S. Pat. Appl. Publ., 34 pp., Cont.-in-part of U.S. Ser. No. 703,140, abandoned.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

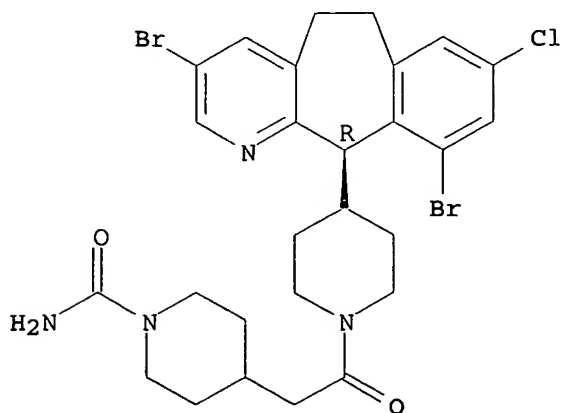
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005101576	A1	20050512	US 2004-841820	20040510
PRIORITY APPLN. INFO.:			US 2003-703140	B2 20031106

AB Methods of treating MDS, or ameliorating a symptom thereof, are disclosed. Specific methods encompass the administration of one or more vitamin D compds., or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with one or more addnl. active agents. Other methods include intermittent administration of a high dose of one or more vitamin D compds., or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with one or more addnl. active agents. Such intermittent administration allows high doses of the vitamin D compds. to be administered while minimizing or eliminating hypercalcemia. Patients having low risk MDS and refractory anemia unresponsive to erythropoietin were entered into a Phase 2 trial to evaluate the effect of high dose pulse administration of calcitriol. Patients were administered weekly oral calcitriol at a dose of 45 µg for 20 consecutive weeks. The calcitriol was formulated in a composition containing the following excipients with the amount given in approx. percentage by weight: 65 % MIGLYOL 812N, 30 % GELUCIRE 44/14, 5 % vitamin-E TPGS and about 0.05 % each of butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA). The high dose pulse administration of calcitriol showed beneficial effect for the treatment of MDS.

IT 193275-84-2, SARASAR
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)

RN 193275-84-2 HCAPLUS
 CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidiny]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:369221 HCAPLUS

DOCUMENT NUMBER: 142:430024

TITLE: Preparation of substituted 2-arylmethylene-N-aryl-N'-aryl-malonamides and analogs as activators of caspases and inducers of apoptosis

INVENTOR(S): Cai, Sui Xiong; Pervin, Azra; Kasibhatla, Shailaja; Nguyen, Bao Ngoc

PATENT ASSIGNEE(S): Cytovia, Inc., USA

SOURCE: PCT Int. Appl., 140 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037196	A2	20050428	WO 2004-US32570	20041005
WO 2005037196	A3	20051013		

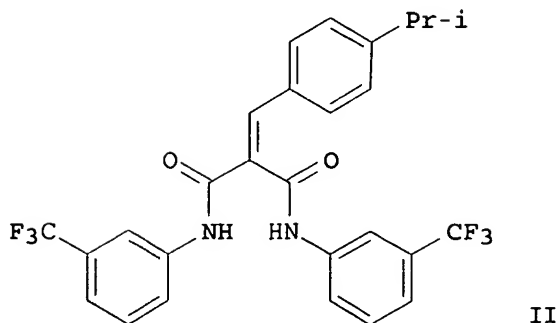
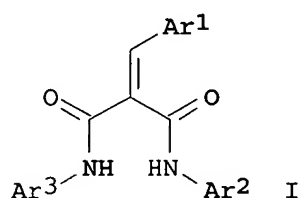
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-508290P P 20031006

OTHER SOURCE(S): MARPAT 142:430024

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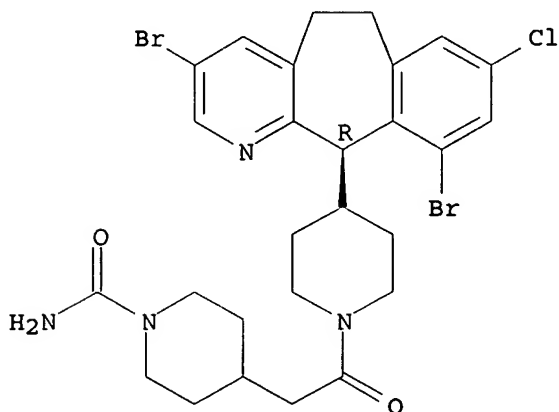
AB Substituted 2-arylmethylene-N-aryl-N'-aryl-malonamides and analogs I [wherein Ar1, Ar2, Ar3 = independently (un)substituted hetero/aryl, hetero/arylalkyl, (partially) saturated carbocyclic, heterocyclic] were prepared as activators of caspases and inducers of apoptosis for treating neoplasm. For example, II was prepared by acylation of with 3-aminobenzotrifluoride malonyl dichloride and reaction of the diamide with 4-isopropylbenzaldehyde. II exhibited caspase activation (EC50 = 15 nM for human breast cancer cell line T-47D), inhibition of cell proliferation (GI50 = 180 nM for T-47D). II induced apoptosis in Jurkat and T-47D cells. I can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs.

IT 193275-84-2, SCH 66336
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (combination therapy; preparation of 2-arylmethylene-N,N'-diarylmalonamides and analogs as activators of caspases and inducers of apoptosis)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:283298 HCAPLUS

DOCUMENT NUMBER: 142:349042

TITLE: Combinations of chlorpromazine compounds and antiproliferative drugs for the treatment of neoplasms

INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzhen; Keith, Curtis

PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA

SOURCE: PCT Int. Appl., 65 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027842	A2	20050331	WO 2004-US30368	20040916
WO 2005027842	A3	20051222		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW,
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
 SN, TD, TG

AU 2004273910 A1 20050331 AU 2004-273910 20040916
 CA 2538570 AA 20050331 CA 2004-2538570 20040916
 EP 1670477 A2 20060621 EP 2004-788798 20040916
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
 NO 2006001325 A 20060606 NO 2006-1325 20060323
 PRIORITY APPLN. INFO.: US 2003-504310P P 20030918
 WO 2004-US30368 W 20040916

OTHER SOURCE(S): MARPAT 142:349042

AB The invention discloses a method for treating a patient having a cancer or other neoplasm by administering chlorpromazine or a chlorpromazine analog and an antiproliferative agent simultaneously or within 14 days of each other in amts. sufficient to treat the patient.

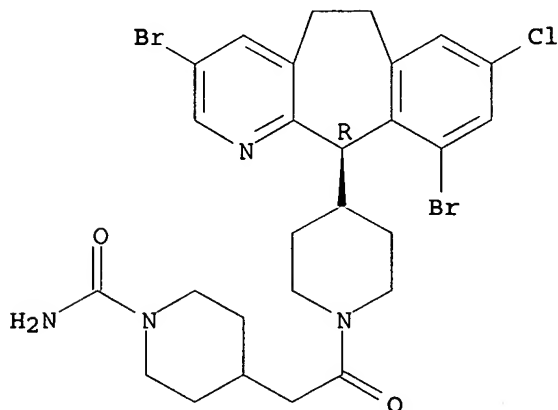
IT 193275-84-2, Lonafarnib

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (chlorpromazine compound-antiproliferative drug antitumor combination)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:63766 HCAPLUS

DOCUMENT NUMBER: 143:53006

TITLE: Hyperleukocytosis complicating lonafarnib treatment in patients with chronic myelomonocytic leukemia

AUTHOR(S): Buresh, A.; Perentesis, J.; Rimsza, L.; Kurtin, S.; Heaton, R.; Sugrue, M.; List, A.

CORPORATE SOURCE: Departments of Medicine and Pathology, The Arizona Cancer Center, University of Arizona College of Medicine, Tucson, AZ, USA

SOURCE: Leukemia (2005), 19(2), 308-310

CODEN: LEUKED; ISSN: 0887-6924

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

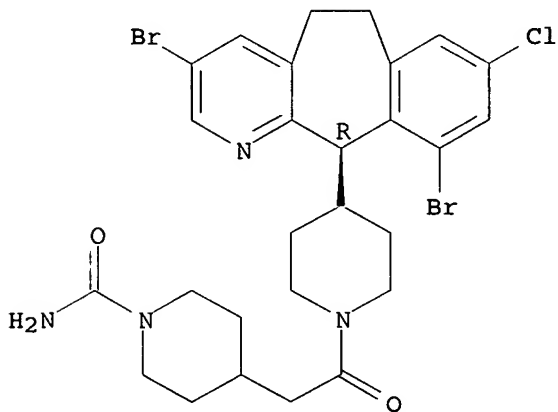
AB Lonafernib is a member of a novel class of therapeutics under investigation in hematol. malignancies, termed the farnesyl transferase inhibitors (FTIs). Three patients with chronic myelomonocytic leukemia (CMML) who developed lonafernib-associated hyperleukocytosis are described. In two cases, lonafernib treatment was also associated with respiratory distress that resolved promptly following treatment with dexamethasone or study drug withdrawal. An infectious etiol. was excluded in both patients presenting with pulmonary infiltrates, whereas cytol. examination of the bronchioalveolar lavage fluid in the other patient confirmed alveolar infiltration by mature monocytes. Despite associated neutrophilia, expansion of a comparatively mature monocytic clone distinguishes these cases from the leukemia differentiation syndrome described with all-trans-retinoic acid treatment of acute promyelocytic leukemia. These cases represent the first description of leukemia differentiation-like syndrome occurring in patients treated with an FTI. Patients with proliferative CMML (white blood cell count above 12,000/ μ l) in particular appear to be at significant risk for this complication.

IT 193275-84-2, Lonafernib
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (farnesyl transferase inhibitor lonafernib caused hyperleukocytosis and pulmonary sequestration syndrome in chronic myelomonocytic leukemia human)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 18 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:895355 HCAPLUS

DOCUMENT NUMBER: 142:211151

TITLE: Clinical Activity of Farnesyl Transferase Inhibitors in Hematologic Malignancies: Possible Mechanisms of Action

AUTHOR(S): Jabbour, Elias; Kantarjian, Hagop; Cortes, Jorge

CORPORATE SOURCE: Department of Leukemia, The University of Texas M.D. Anderson Cancer Center, Houston, TX, 77030, USA

SOURCE: Leukemia & Lymphoma (2004), 45(11), 2187-2195

CODEN: LELYEA; ISSN: 1042-8194

PUBLISHER: Taylor & Francis Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Farnesyl transferase inhibitors (FTIs) are a novel class of anti-cancer agents that competitively inhibit farnesyl protein transferase (FTase). Initially developed to inhibit the prenylation necessary for Ras activation, their mechanism of action seems to be more complex, involving other proteins unrelated to Ras. FTIs have been developed and tested across a wide range of human cancers. At least 3 agents within this family have been investigated in hematol. malignancies. These are tipifarnib (R115777, Zarnestra), lonafarnib (SCH66336, SarasarTM), both of which are orally administered, and BMS-214662, which is given i.v. Preliminary results from clin. trials demonstrate enzyme target inhibition, a favorable toxicity profile and promising efficacy. Ongoing studies will better determine their mechanism of action and the role of combination with other agents, defining their place in the therapeutic arsenal of hematol. disorders.

IT 193275-84-2, Sarasar

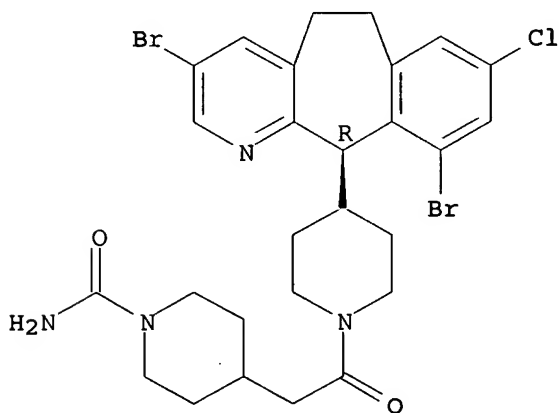
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(clin. trials with farnesyl transferase inhibitor lonafarnib demonstrated enzyme target inhibition, favorable toxicity profile and promising efficacy in hematol. malignancies)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 19 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:756710 HCAPLUS

DOCUMENT NUMBER: 141:277628

TITLE: Preparation of ureidophenoxycyanopyridines as anticancer drugs.

INVENTOR(S): Scott, William J.; Dumas, Jacques; Boyer, Stephen; Lee, Wendy; Chen, Yuanwei; Phillips, Barton; Verma, Sharad; Chen, Jianqing; Chen, Zhi; Fan, Jianmei; Raudenbush, Brian; Redman, Aniko; Yi, Lin; Zhu, Qingming

PATENT ASSIGNEE(S): Bayer Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 127 pp.

CODEN: PIXXD2

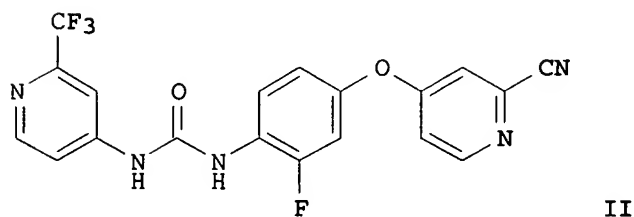
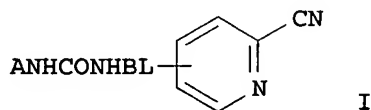
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

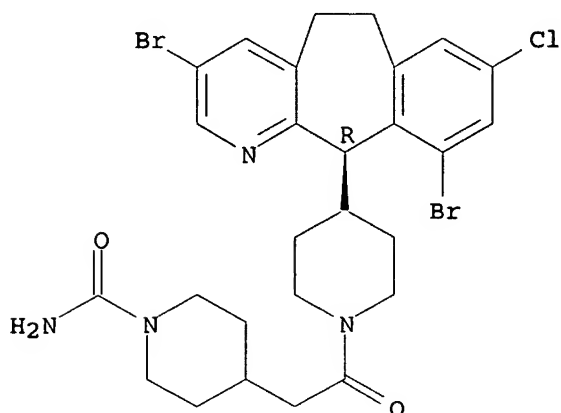
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078747	A1	20040916	WO 2004-US6286	20040301
WO 2004078747	C1	20041104		
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US 2004235829	A1	20041125	US 2004-788029	20040227
AU 2004217977	A1	20040916	AU 2004-217977	20040301
CA 2517361	AA	20040916	CA 2004-2517361	20040301
US 2004229937	A1	20041118	US 2004-789446	20040301
US 2005032798	A1	20050210	US 2004-788405	20040301
US 2005038031	A1	20050217	US 2004-788426	20040301
EP 1599467	A1	20051130	EP 2004-716144	20040301
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004007897	A	20060301	BR 2004-7897	20040301
JP 2006519264	T2	20060824	JP 2006-508977	20040301
PRIORITY APPLN. INFO.:			US 2003-450323P	P 20030228
			US 2003-450324P	P 20030228
			US 2003-450348P	P 20030228
			WO 2004-US6286	A 20040301
OTHER SOURCE(S): MARPAT 141:277628				
GI				



- AB Title compds. [I; A = (substituted) pyridinyl, naphthyl, 8-10 membered bicyclic heteroaryl, heterocyclyl, carbocyclyl; B = (substituted) phenylene, naphthylenediyl; L = O, S; m = 0-3; R2 = alkyl, haloalkyl, alkoxy, N-oxo, N-hydroxy], were prepared Thus, 2-trifluoromethyl-4-pyridylamine was stirred 20 h with carbonyldiimidazole in CH₂Cl₂; 4-(4-amino-3-fluorophenoxy)pyridine-2-carbonitrile (preparation given) was added followed by stirring for 1 day to give 75% title compound (II). I inhibited c-RAF-1 kinase with IC₅₀ = 7.86 nM to >1600 nM.
- IT 193275-84-2, Lonafarnib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of ureidophenoxycyanopyridines as anticancer drugs)
- RN 193275-84-2 HCAPLUS
- CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-

(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 20 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:565086 HCAPLUS

DOCUMENT NUMBER: 141:123632

TITLE: Preparation of 3,5-Disubstituted-[1,2,4]-oxadiazoles and analogs as activators of caspases and inducers of apoptosis

INVENTOR(S): Cai, Sui Xiong; Zhang, Han-zhong; Kuemmerle, Jared D.; Zhang, Hong; Kemnitzer, William E.

PATENT ASSIGNEE(S): Cytovia, Inc., USA

SOURCE: PCT Int. Appl., 97 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

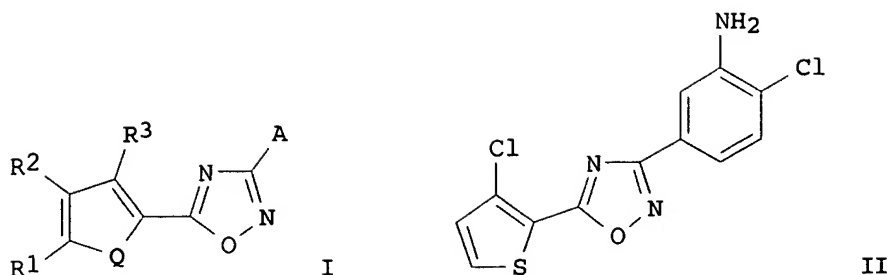
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058253	A1	20040715	WO 2003-US40308	20031218
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004127521	A1	20040701	US 2003-737865	20031218
CA 2509224	AA	20040715	CA 2003-2509224	20031218
AU 2003303373	A1	20040722	AU 2003-303373	20031218
EP 1581213	A1	20051005	EP 2003-808469	20031218
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1756547	A	20060405	CN 2003-80106440	20031218
JP 2006516250	T2	20060629	JP 2004-563731	20031218
PRIORITY APPLN. INFO.:			US 2002-433953P	P 20021218
			WO 2003-US40308	W 20031218

OTHER SOURCE(S): MARPAT 141:123632

GI



AB Title compds. I [R1-3 = H, halo, haloalkyl, aryl, etc.; Q = S, O, amino; A = heterocycle, carbocycle] are prepared For instance, 3-amino-4-chlorobenzamidoxime (preparation given) is reacted with 3-chlorothiophene-2-carbonyl chloride (pyridine, reflux, 50 min) to give II. II and other examples are potent caspase cascade activators and inducers of apoptosis in solid tumor cells, e.g., human breast cancer cell lines T-47D and ZR-75-1.

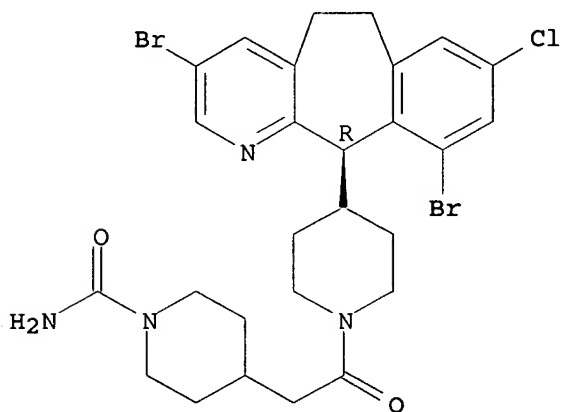
IT 193275-84-2, SCH66336

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of 3,5-Disubstituted-[1,2,4]-oxadiazoles and analogs as activators of caspases and inducers of apoptosis)

RN 193275-84-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11R)-3,10-dibromo-8-chloro-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperidinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:559502 HCAPLUS

DOCUMENT NUMBER: 141:190802

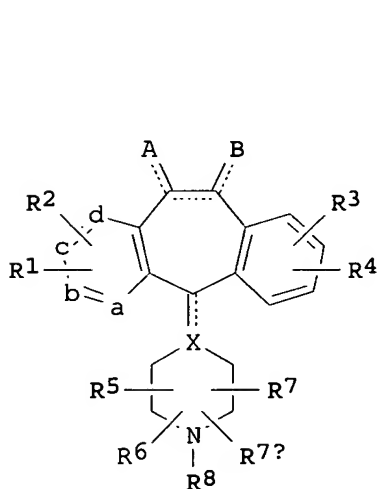
TITLE: Preparation of tricyclic antitumor compounds as farnesyl protein transferase inhibitors

INVENTOR(S): Zhu, Hugh Y.; Njoroge, F. George; Cooper, Alan B.; Guzi, Timothy; Rane, Dinanath F.; Minor, Keith P.; Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Santhanam, Bama; Pinto, Patrick A.; Vibulbhan, Bancha; Keertikar, Kartik M.; Alvarez, Carmen S.; Baldwin, John J.; Li, Ge; Huang, Chia-yu; James, Ray A.;

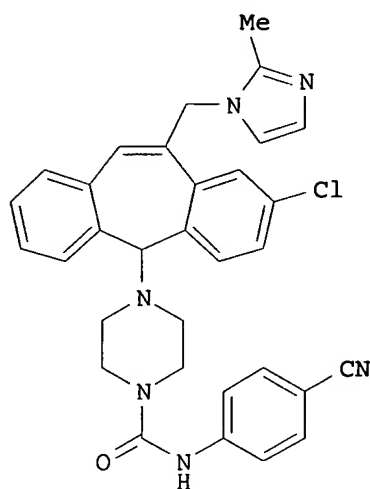
Bishop, W. Robert; Wang, James J.-S.; Desai, Jagdish A.
 PATENT ASSIGNEE(S): Schering Corporation, USA
 SOURCE: U.S. Pat. Appl. Publ., 731 pp., Cont.-in-part of U.S. Ser. No. 85,896.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 6
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004122018	A1	20040624	US 2002-325896	20021219
US 2002198216	A1	20021226	US 2001-940811	20010828
US 2003229099	A1	20031211	US 2002-85896	20020227
US 2004122018	A1	20040624	US 2002-325896	20021219
PRIORITY APPLN. INFO.:			US 2001-940811	A2 20010828
			US 2002-85896	A2 20020227
			US 2002-325896	A 20021219
			US 2000-229183P	P 20000830

GI



I



II

AB Title benzo[5,6]cyclohepta[1,2-b]pyridines and analogs (I) [wherein one of a, b, d, e = N, N=O; remaining a, b, d, e = C substituted with R1 or R2; or each a, b, d, e = C substituted with R1 or R2; X = N, C, CH; A, B = independently H, (un)substituted R9, carbamoyl(alkyl), amino(alkyl), acylamino(alkyl), ureido(alkyl), etc.; R1-R4 = independently H, halo, CF3, alkoxy, amino, NO2, CN, alkyl, alkenyl, alkynyl, etc.; R5-R7a = independently H, CF3, acyl, alkyl, aryl; R8 = H, alkoxycarbonyl, aryloxy, carbonyl, alkylsulfonyl, arylsulfonyl, etc.; R9 = (un)substituted heteroaryl(alkyl), arylalkoxy, heterocyclyl(alkyl), etc.; and stereoisomers, pharmaceutically acceptable salts, solvates, and prodrugs thereof] were prepared as farnesyl protein transferase (FPT) inhibitors. For example, a multi-step synthesis starting from tert-Bu 4-[8-chloro-6-(hydroxymethyl)-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinecarboxylate, 2-methylimidazole, and p-cyanophenyl isocyanate gave (S)-II. The latter inhibited tumor growth of mouse H-Ras fibroblasts, HTB-177 human non-small cell lung cancer cells, and LOX human melanoma cells by 98% (60 MPK, p.o., BID, x2), 96% (80 MPK, p.o., BID, x3), and 90.3% (60 MPK, p.o., BID, x1), resp. Compds. of the invention

inhibited FPT activity with IC50 values in the range of 0.05 nM to 100 nM and suppressed anchorage-independent growth of human tumor cells in a soft agar assay with IC50 values in the range of <0.5 nM to 50 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of proliferative diseases, such as cancer.

IT 740819-70-9P 740819-71-0P 740819-72-1P
 740819-73-2P 740819-74-3P 740819-75-4P
 740819-76-5P 740819-77-6P 740819-78-7P
 740819-79-8P 740819-80-1P 740819-81-2P
 740819-82-3P 740819-83-4P 740819-84-5P
 740819-85-6P 740819-86-7P 740819-87-8P
 740819-88-9P 740819-89-0P 740819-90-3P
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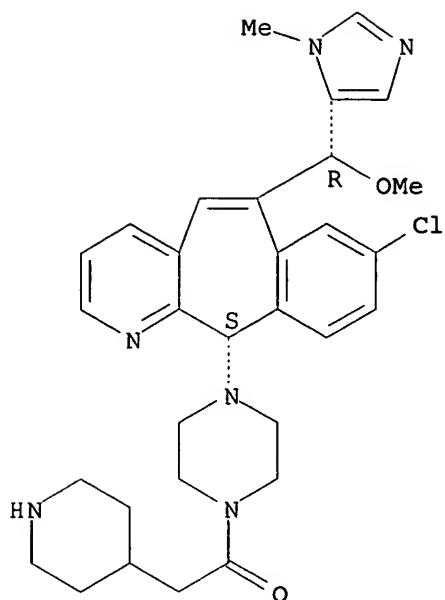
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(FPT inhibitor; preparation of tricyclic antitumor agents as farnesyl protein transferase inhibitors for treatment of cancer and other proliferative diseases)

RN 740819-70-9 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

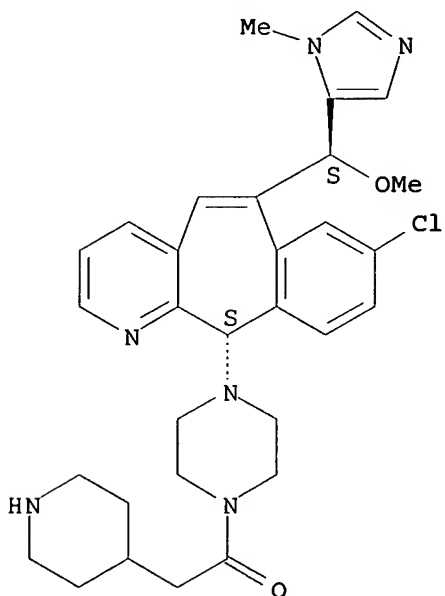
Absolute stereochemistry.



RN 740819-71-0 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

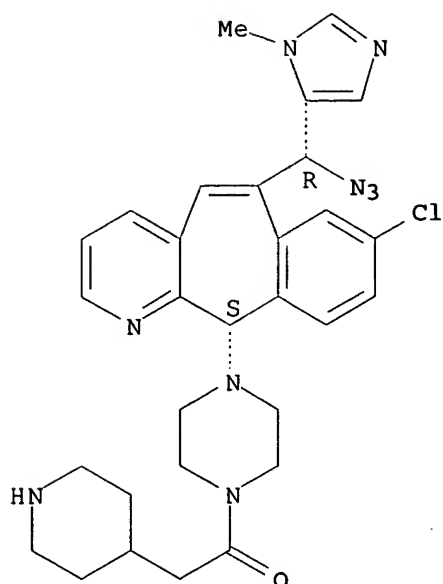
Absolute stereochemistry.



RN 740819-72-1 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(R)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

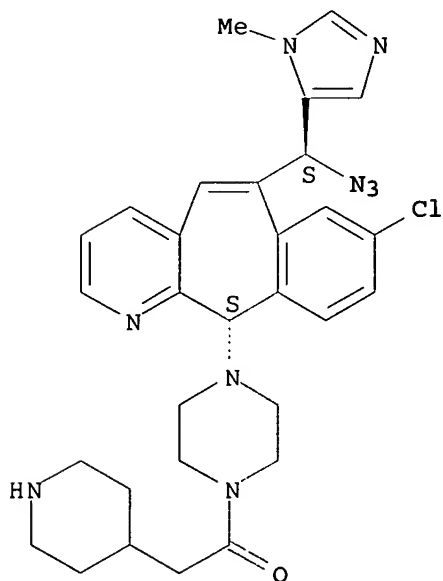
Absolute stereochemistry.



RN 740819-73-2 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(S)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

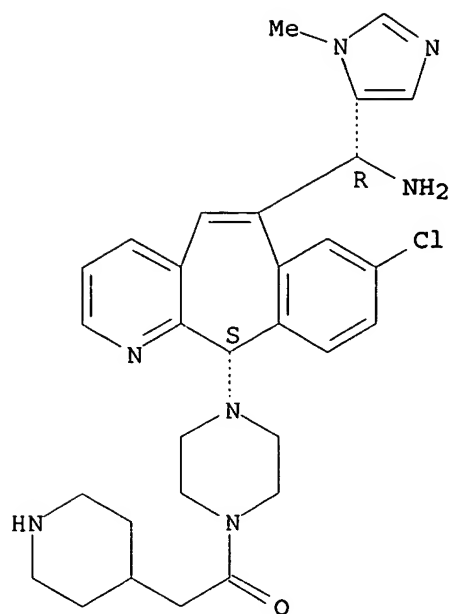
Absolute stereochemistry.



RN 740819-74-3 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(R)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

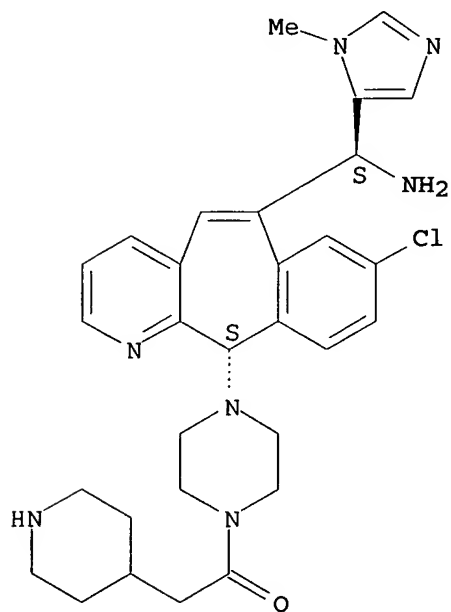
Absolute stereochemistry.



RN 740819-75-4 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(S)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

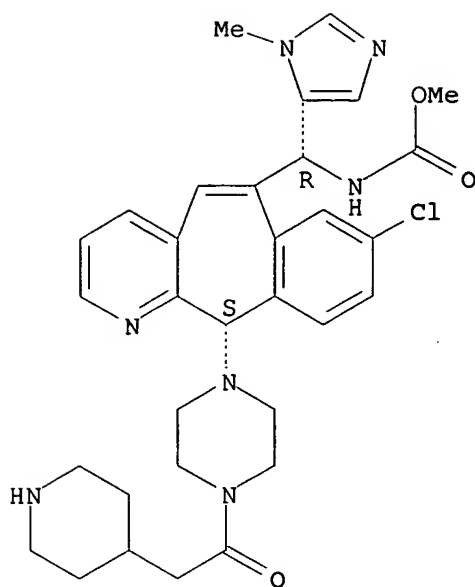
Absolute stereochemistry.



RN 740819-76-5 HCAPLUS

CN Carbamic acid, [(R)-[(11S)-8-chloro-11-[4-(4-piperidinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

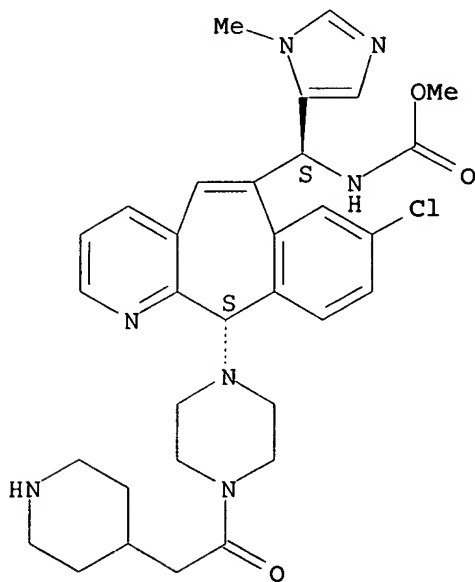
Absolute stereochemistry.



RN 740819-77-6 HCAPLUS

CN Carbamic acid, [(S)-[(11S)-8-chloro-11-[4-(4-piperidinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

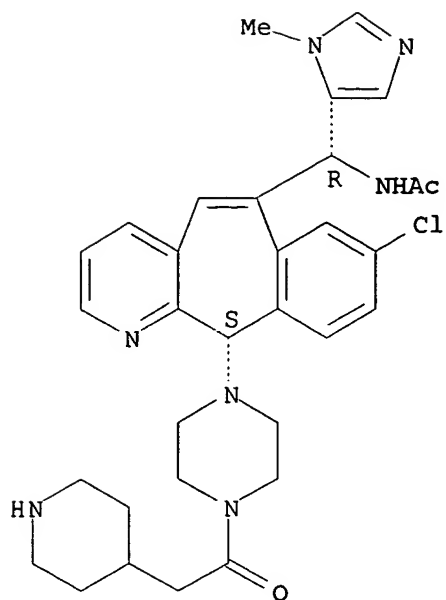
Absolute stereochemistry.



RN 740819-78-7 HCAPLUS

CN Acetamide, N-[(R)-[(11S)-8-chloro-11-[4-(4-piperidinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]- (9CI) (CA INDEX NAME)

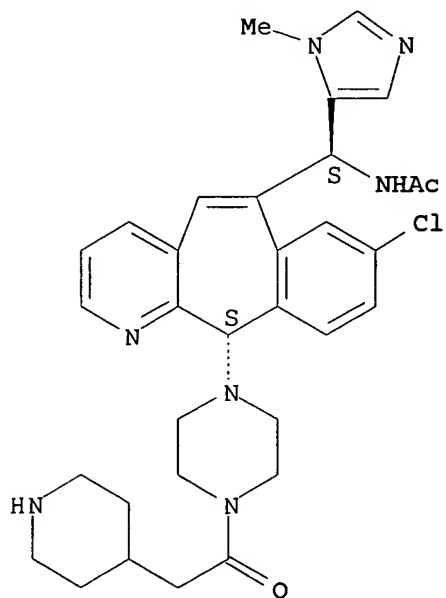
Absolute stereochemistry.



RN 740819-79-8 HCAPLUS

CN Acetamide, N-[(S)-[(11S)-8-chloro-11-[4-(4-piperidinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]- (9CI) (CA INDEX NAME)

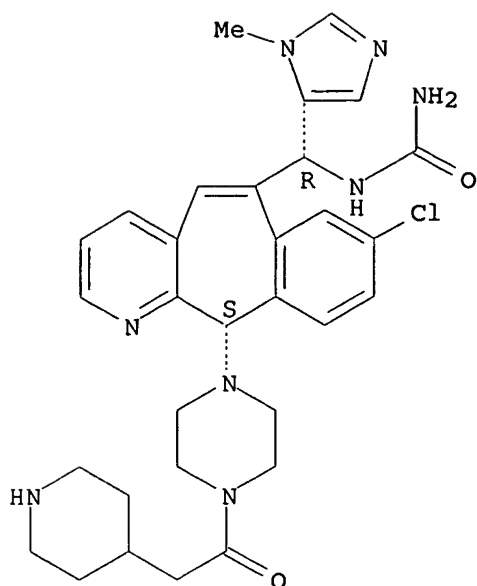
Absolute stereochemistry.



RN 740819-80-1 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(R)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

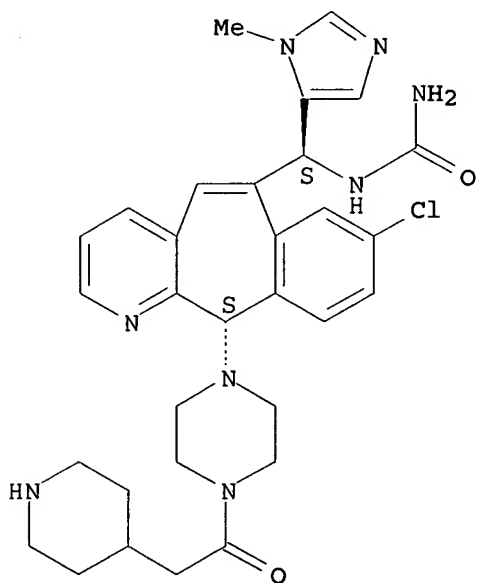
Absolute stereochemistry.



RN 740819-81-2 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(S)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11'-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

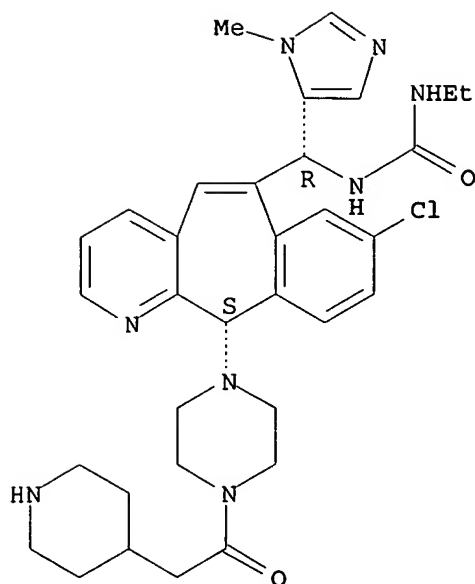
Absolute stereochemistry.



RN 740819-82-3 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11'-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

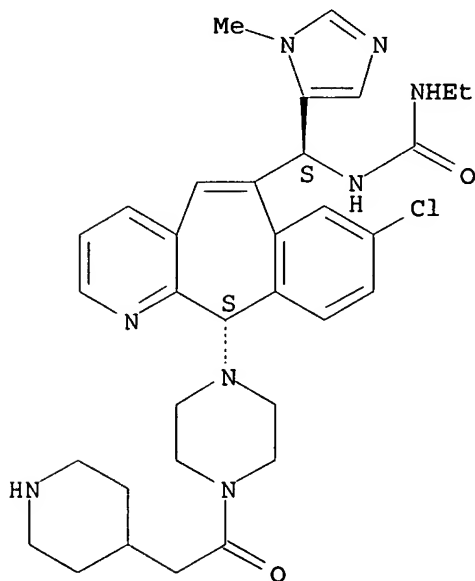
Absolute stereochemistry.



RN 740819-83-4 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)-(9CI) (CA INDEX NAME)

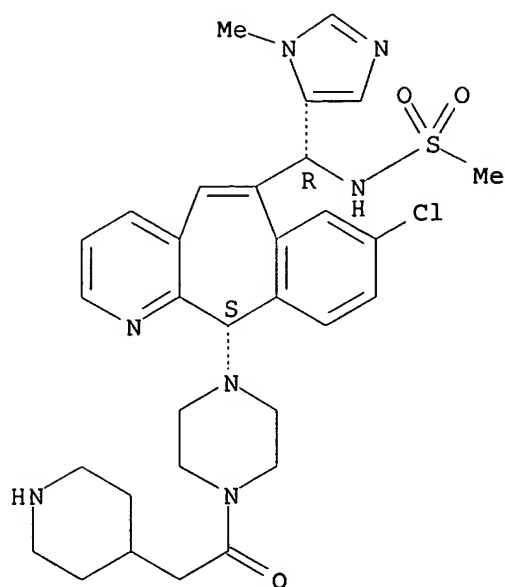
Absolute stereochemistry.



RN 740819-84-5 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[(1-methyl-1H-imidazol-5-yl)[(methylsulfonyl)amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)-(9CI) (CA INDEX NAME)

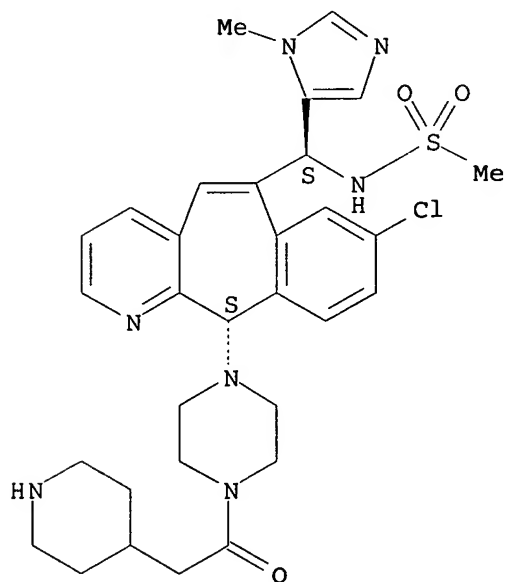
Absolute stereochemistry.



RN 740819-85-6 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-(1-methyl-1H-imidazol-5-yl)[(methylsulfonyl)amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

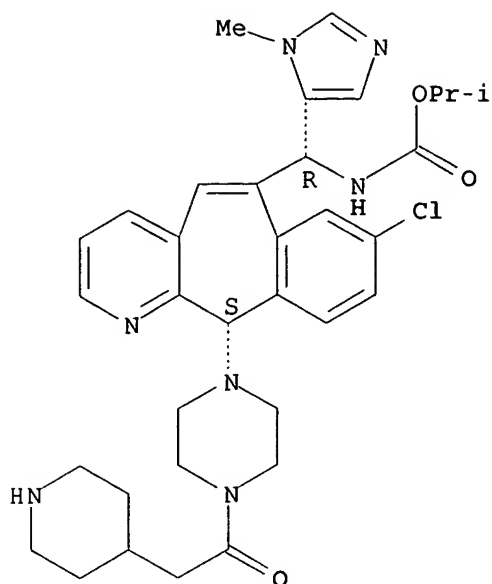
Absolute stereochemistry.



RN 740819-86-7 HCAPLUS

CN Carbamic acid, [(R)-[(11S)-8-chloro-11-[4-(4-piperidinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

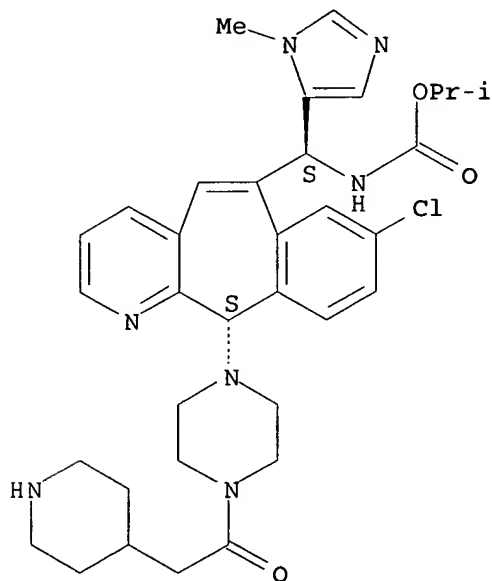
Absolute stereochemistry.



RN 740819-87-8 HCAPLUS

CN Carbamic acid, [(S)-[(11S)-8-chloro-11-[4-(4-piperidinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

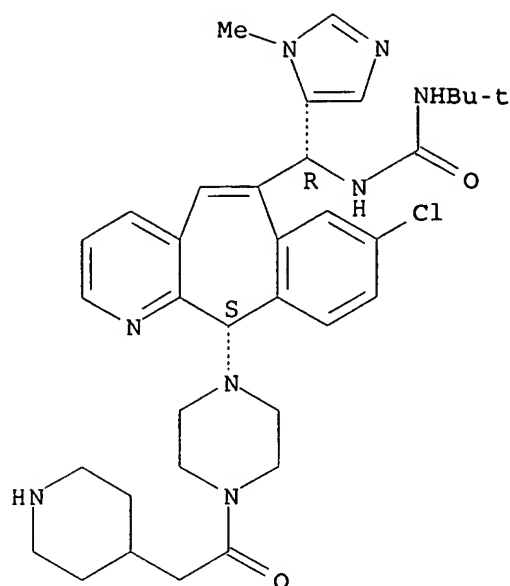
Absolute stereochemistry.



RN 740819-88-9 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

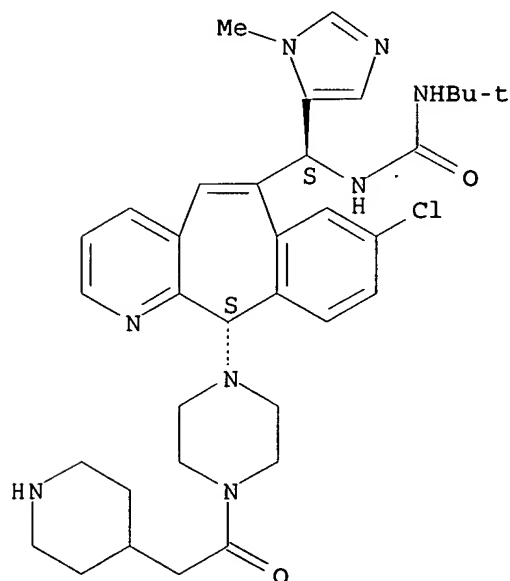
Absolute stereochemistry.



RN 740819-89-0 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)-(9CI) (CA INDEX NAME)

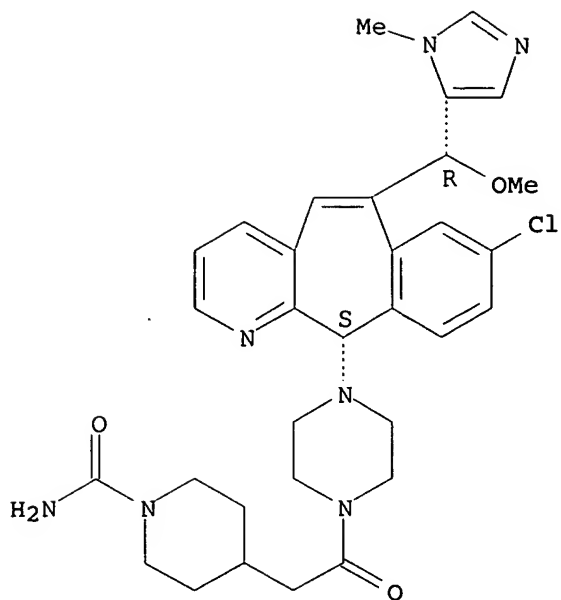
Absolute stereochemistry.



RN 740819-90-3 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(R)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

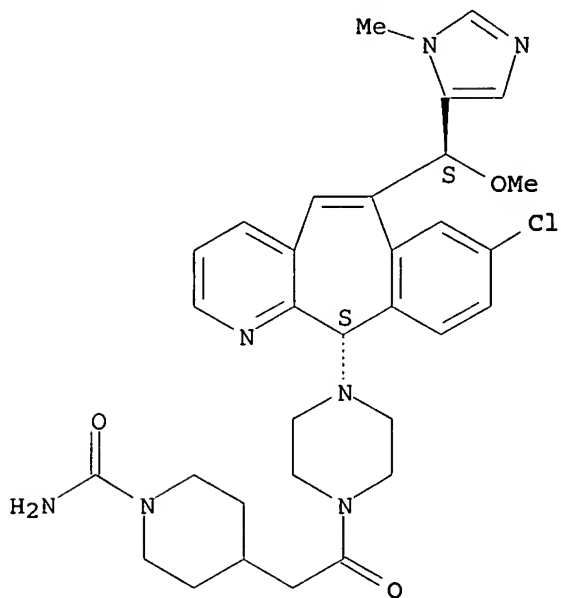
Absolute stereochemistry.



RN 740819-91-4 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(S)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

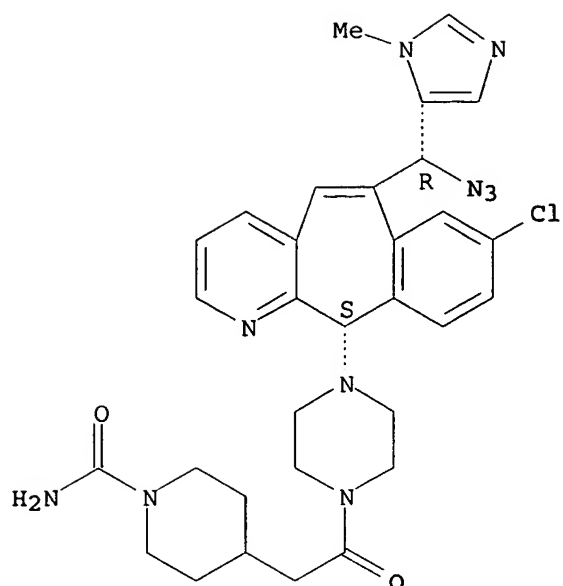
Absolute stereochemistry.



RN 740819-92-5 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-6-[(R)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

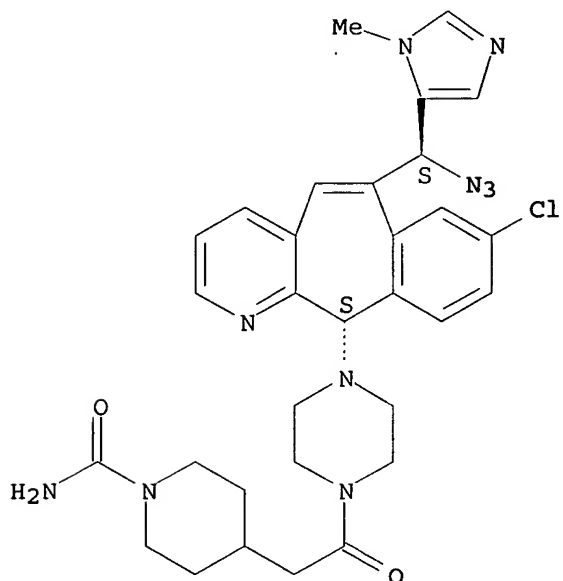
Absolute stereochemistry.



RN 740819-93-6 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(1S)-6-[(S)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

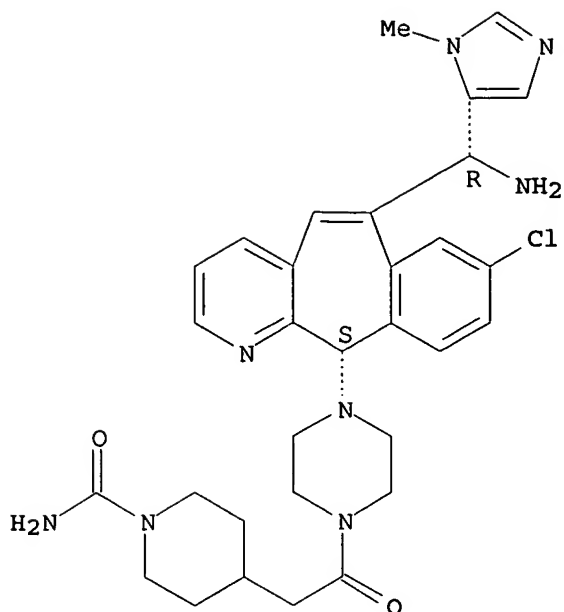
Absolute stereochemistry.



RN 740819-94-7 HCAPLUS

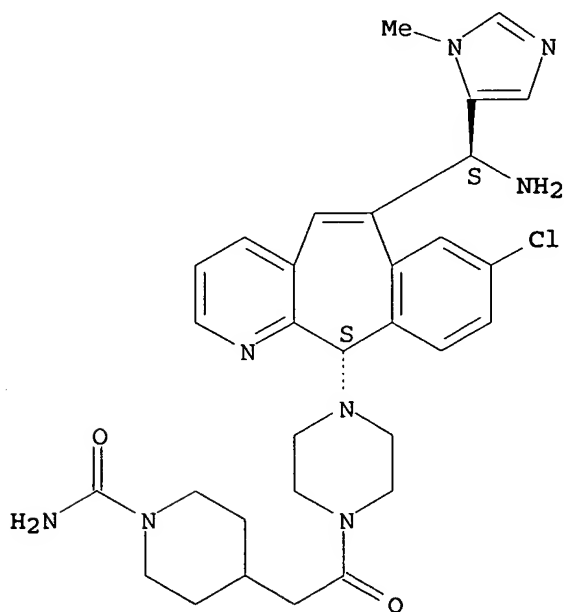
CN 1-Piperidinecarboxamide, 4-[2-[4-[(1S)-6-[(R)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



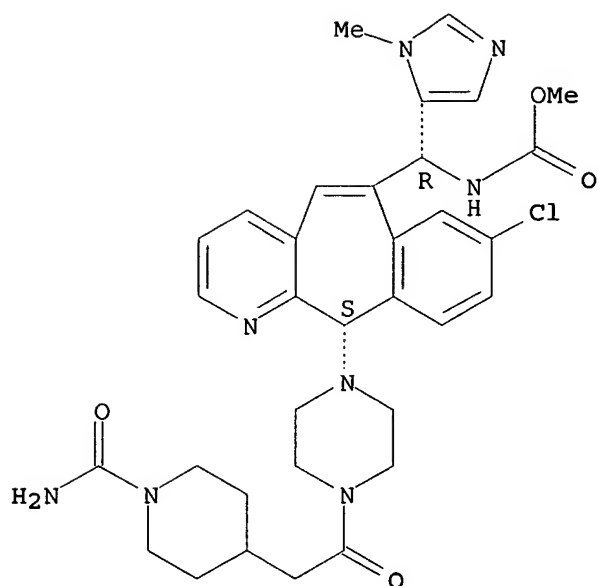
RN 740819-96-9 HCAPLUS
 CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-6-[(S)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 740819-97-0 HCAPLUS
 CN Carbamic acid, [(R)-[(11S)-11-[4-[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-1-piperazinyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

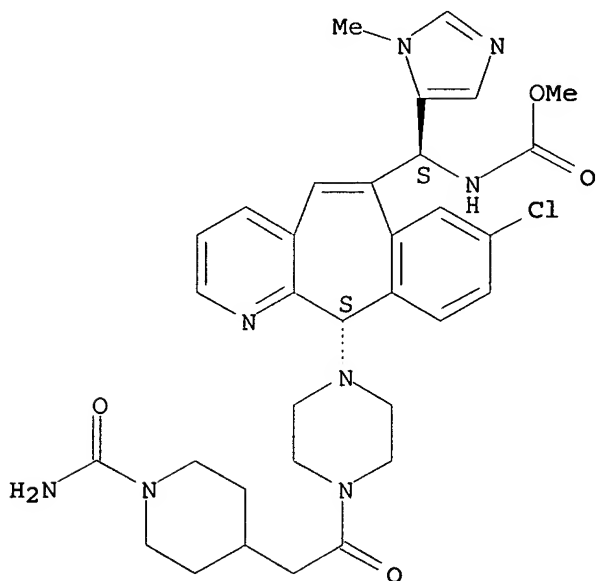
Absolute stereochemistry.



RN 740819-98-1 HCAPLUS

CN Carbamic acid, [(S)-[(11S)-11-[4-[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-1-piperazinyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

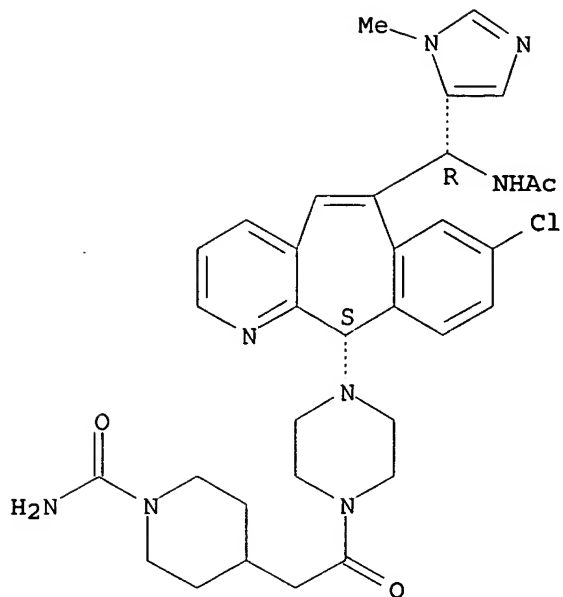
Absolute stereochemistry.



RN 740819-99-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-6-[(R)-(acetylamino)(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

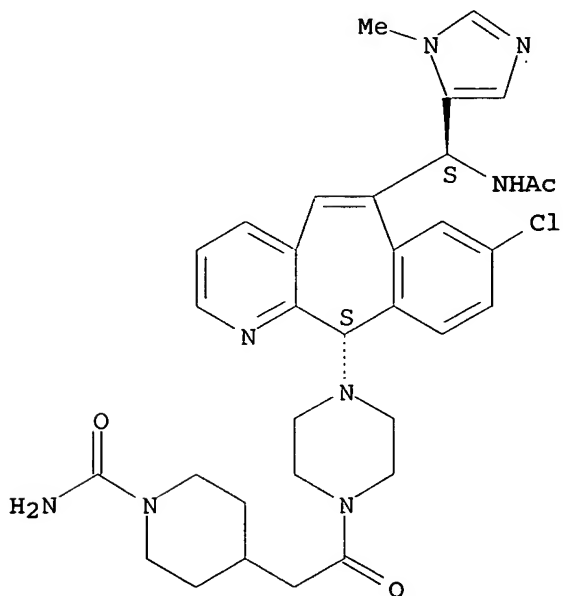
Absolute stereochemistry.



RN 740820-00-2 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-6-[(S)-(acetylamino)(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

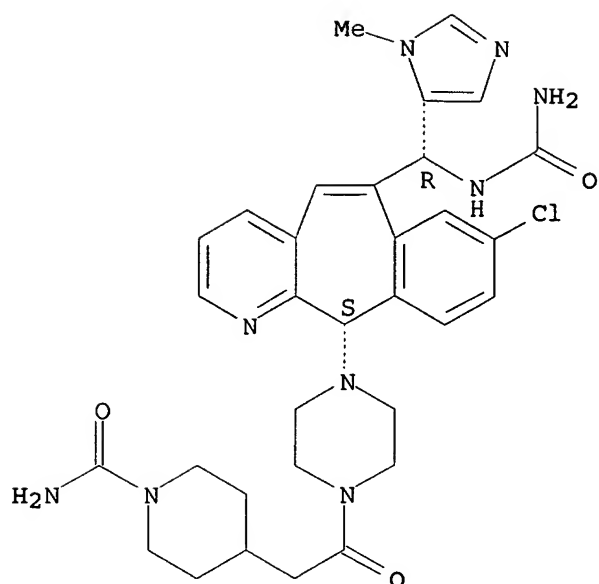
Absolute stereochemistry.



RN 740820-01-3 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-6-[(R)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

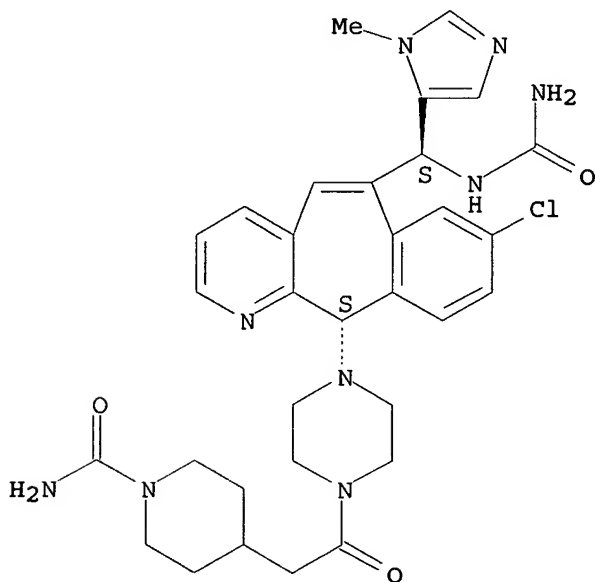
Absolute stereochemistry.



RN 740820-02-4 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-6-[(S)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

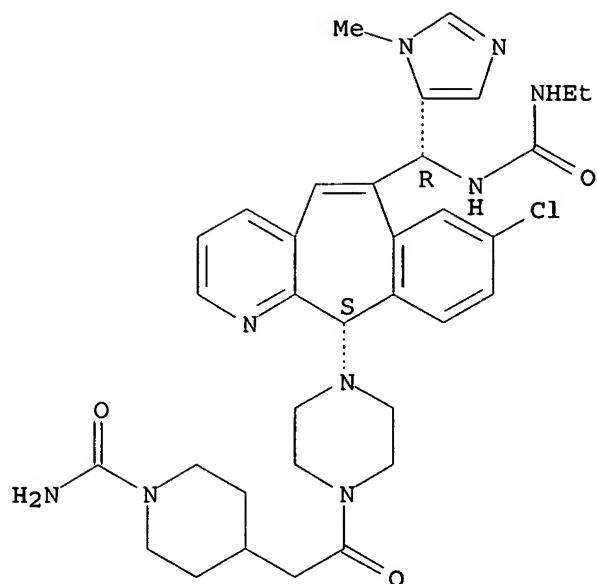
Absolute stereochemistry.



RN 740820-03-5 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(R)-[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

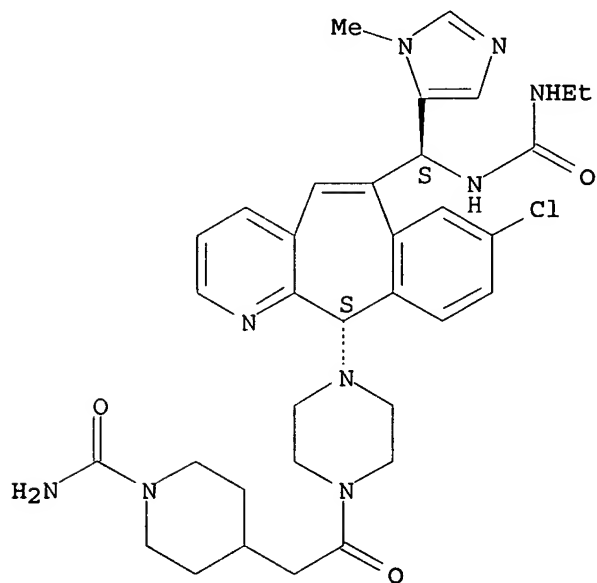
Absolute stereochemistry.



RN 740820-04-6 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(S)-
 [[(ethylamino) carbonyl] amino] (1-methyl-1H-imidazol-5-yl)methyl]-11H-
 benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]-
 (9CI) (CA INDEX NAME)

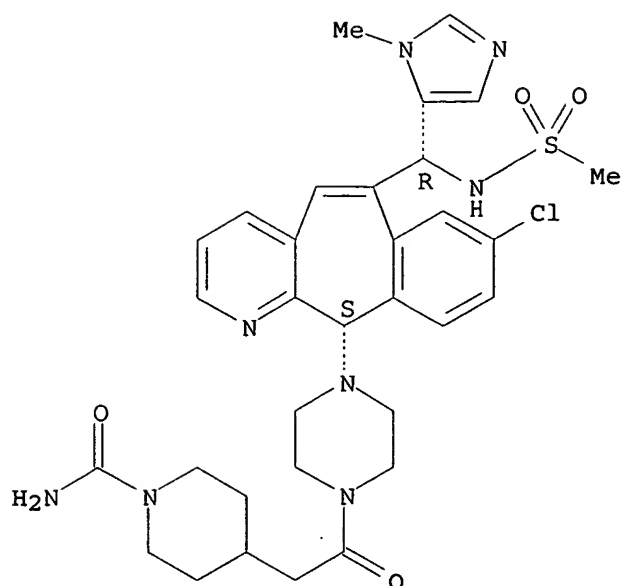
Absolute stereochemistry.



RN 740820-05-7 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(R)- (1-methyl-1H-
 imidazol-5-yl) [(methylsulfonyl) amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-
 b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

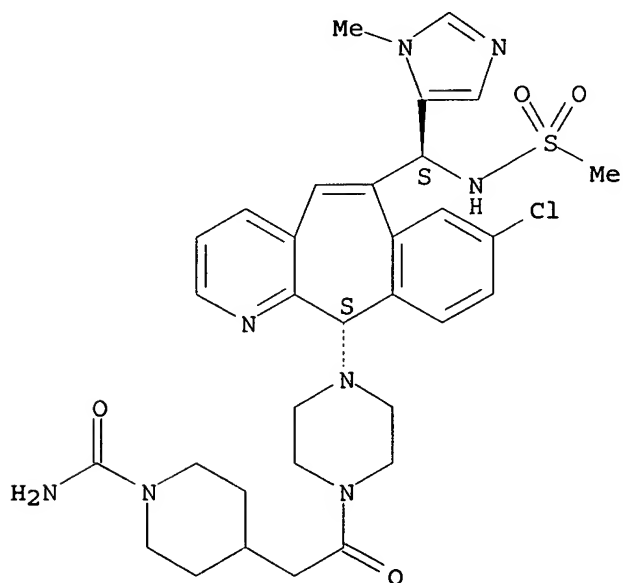
Absolute stereochemistry.



RN 740820-06-8 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(S)-(1-methyl-1H-imidazol-5-yl) [(methylsulfonyl) amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

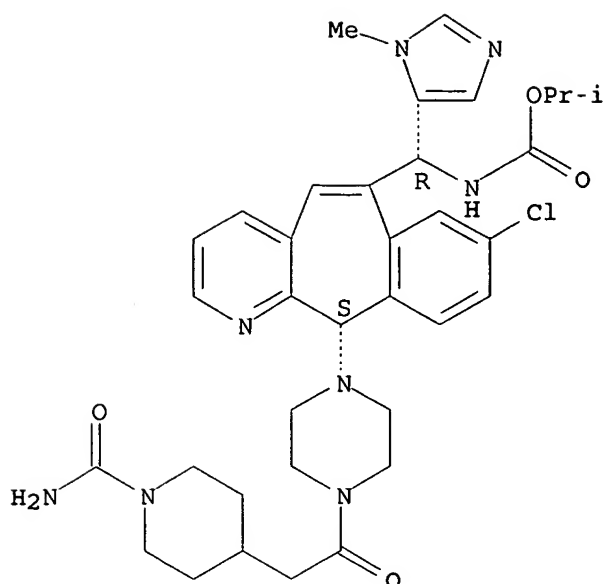
Absolute stereochemistry.



RN 740820-07-9 HCAPLUS

CN Carbamic acid, [(R)-[(11S)-11-[4-[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-1-piperazinyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

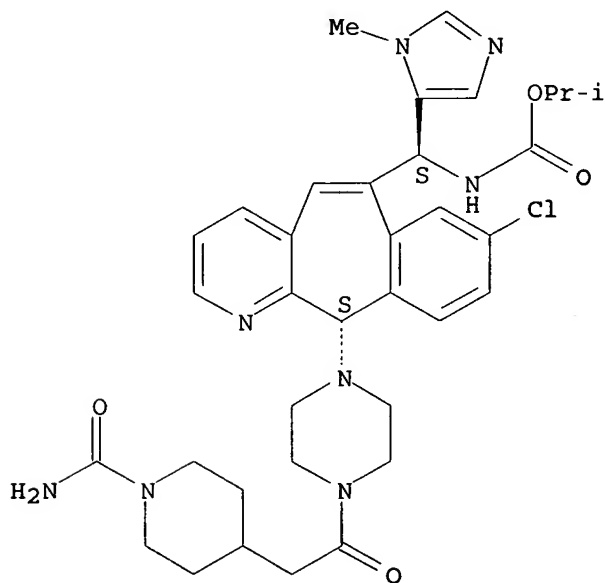
Absolute stereochemistry.



RN 740820-08-0 HCAPLUS

CN Carbamic acid, [(S)-[(11S)-11-[4-[[1-(aminocarbonyl)-4-piperidinyl]acetyl]-1-piperazinyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

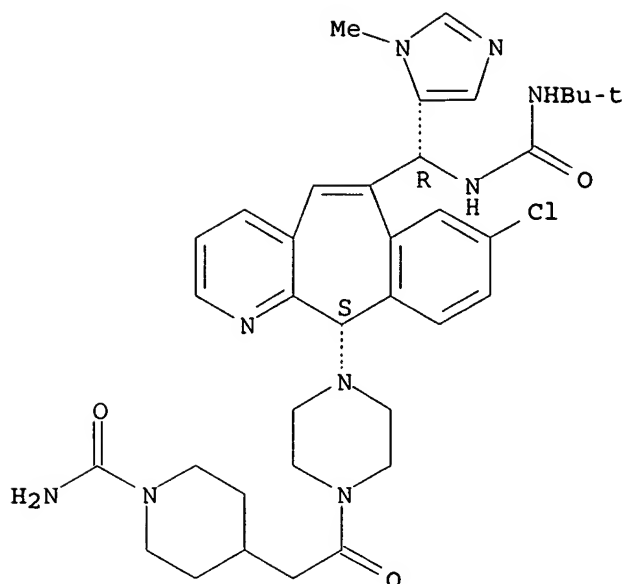
Absolute stereochemistry.



RN 740820-09-1 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(R)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

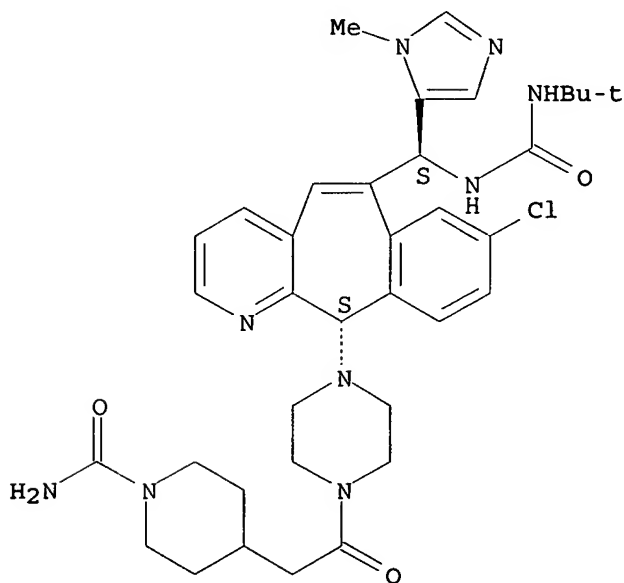
Absolute stereochemistry.



RN 740820-10-4 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[(S)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

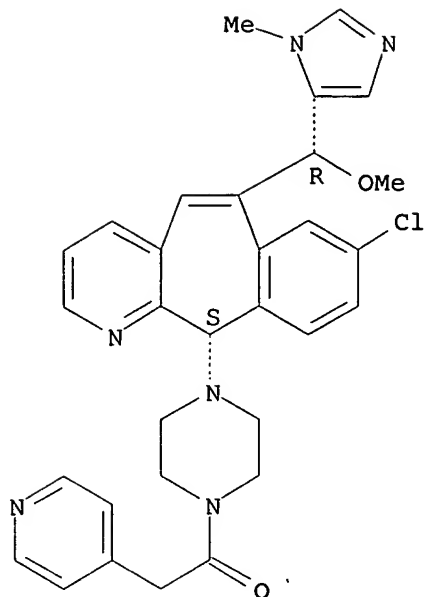
Absolute stereochemistry.



RN 740821-99-2 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

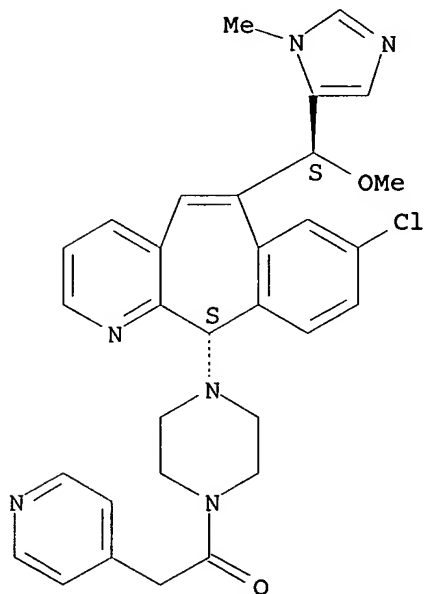
Absolute stereochemistry.



RN 740822-00-8 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

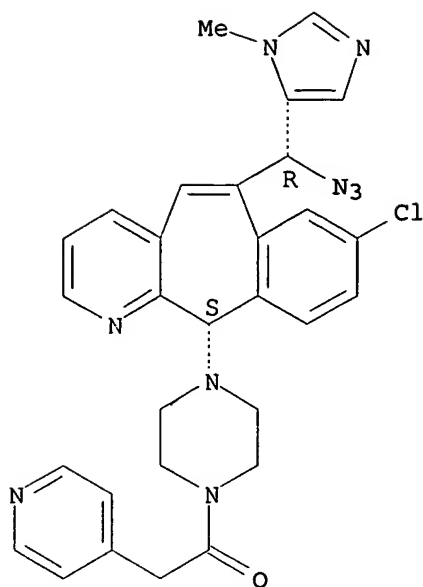
Absolute stereochemistry.



RN 740822-01-9 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(R)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

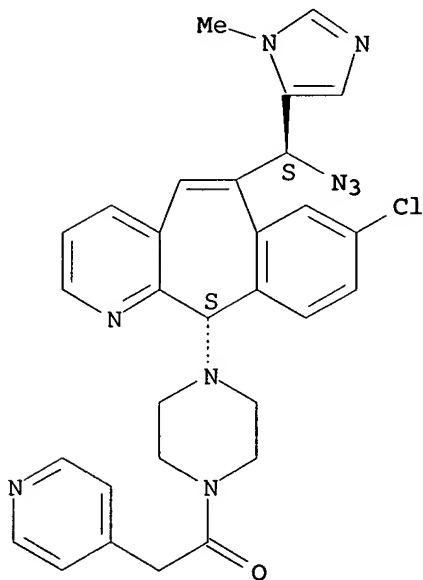
Absolute stereochemistry.



RN 740822-02-0 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(S)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)-(9CI) (CA INDEX NAME)

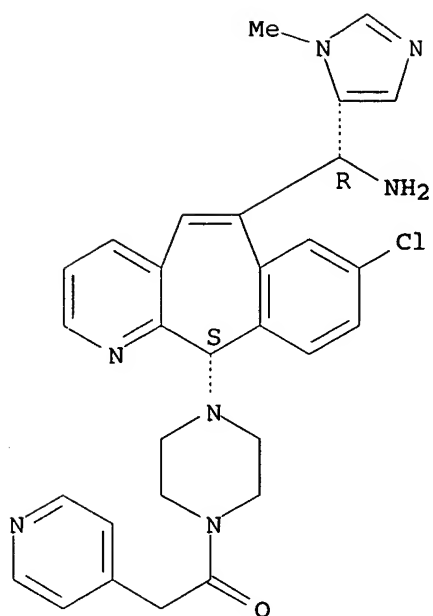
Absolute stereochemistry.



RN 740822-03-1 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(R)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)-(9CI) (CA INDEX NAME)

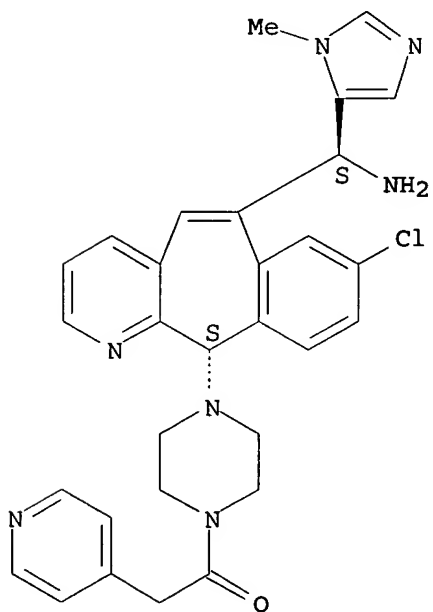
Absolute stereochemistry.



RN 740822-04-2 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(S)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)-(9CI) (CA INDEX NAME)

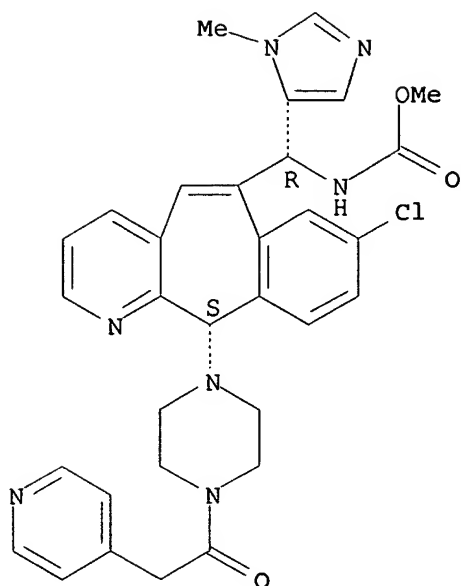
Absolute stereochemistry.



RN 740822-05-3 HCAPLUS

CN Carbamic acid, [(R)-[(11S)-8-chloro-11-[4-(4-pyridinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

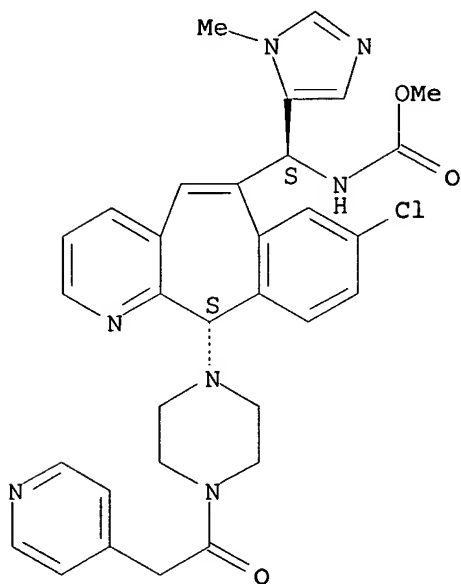
Absolute stereochemistry.



RN 740822-06-4 HCAPLUS

CN Carbamic acid, [(S)-[(11S)-8-chloro-11-[4-(4-pyridinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

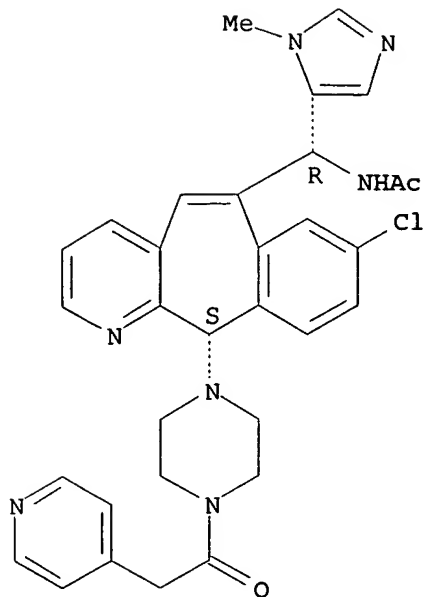
Absolute stereochemistry.



RN 740822-07-5 HCAPLUS

CN Acetamide, N-[(R)-[(11S)-8-chloro-11-[4-(4-pyridinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]- (9CI) (CA INDEX NAME)

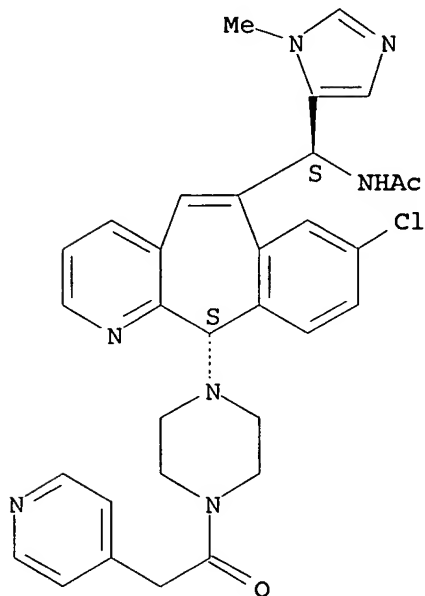
Absolute stereochemistry.



RN 740822-08-6 HCAPLUS

CN Acetamide, N-[(S)-6-[(R)-[1-(4-pyridinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]- (9CI) (CA INDEX NAME)

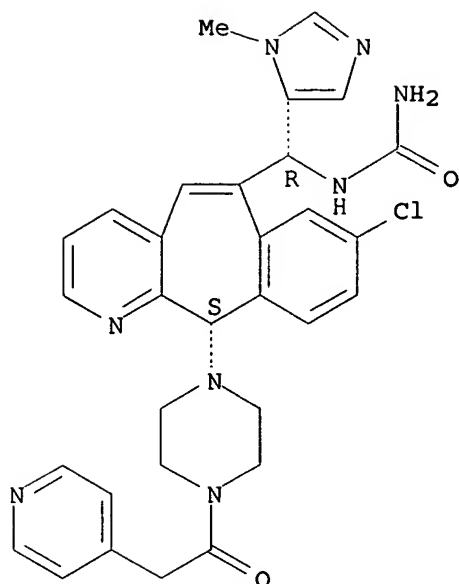
Absolute stereochemistry.



RN 740822-09-7 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(R)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

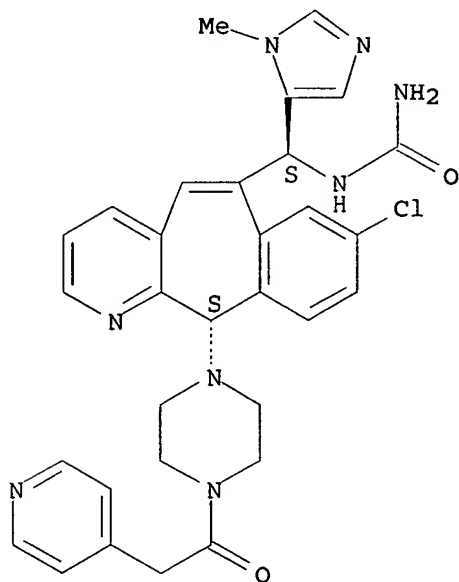
Absolute stereochemistry.



RN 740822-10-0 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(S)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)-(9CI) (CA INDEX NAME)

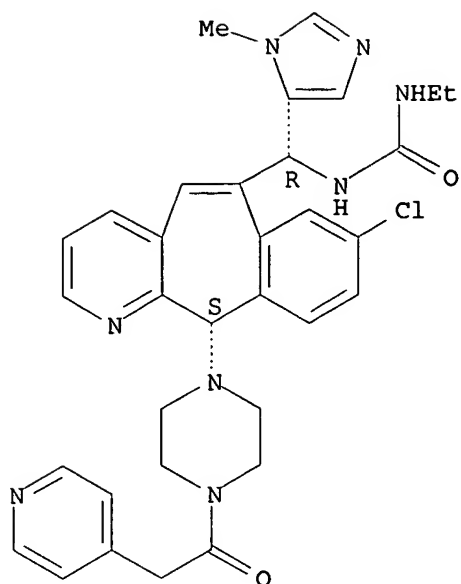
Absolute stereochemistry.



RN 740822-11-1 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)-(9CI) (CA INDEX NAME)

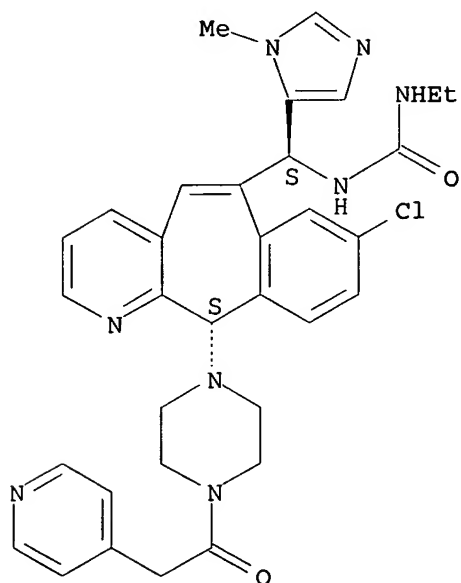
Absolute stereochemistry.



RN 740822-12-2 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

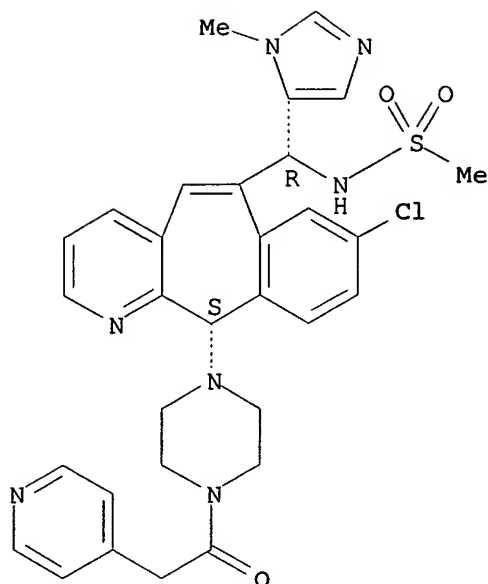
Absolute stereochemistry.



RN 740822-13-3 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[(1-methyl-1H-imidazol-5-yl)[(methylsulfonyl)amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

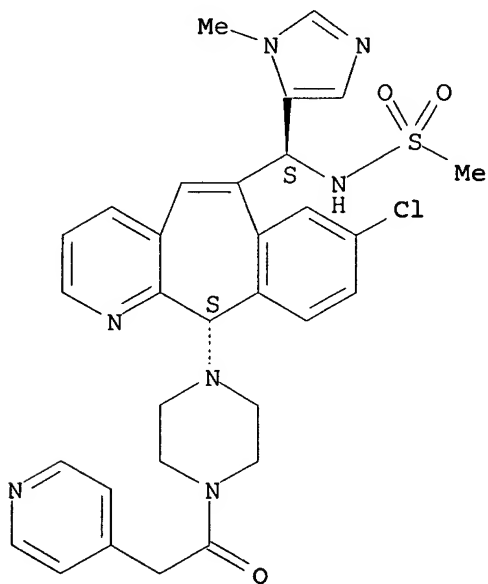
Absolute stereochemistry.



RN 740822-14-4 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-(1-methyl-1H-imidazol-5-yl)[(methylsulfonyl)amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

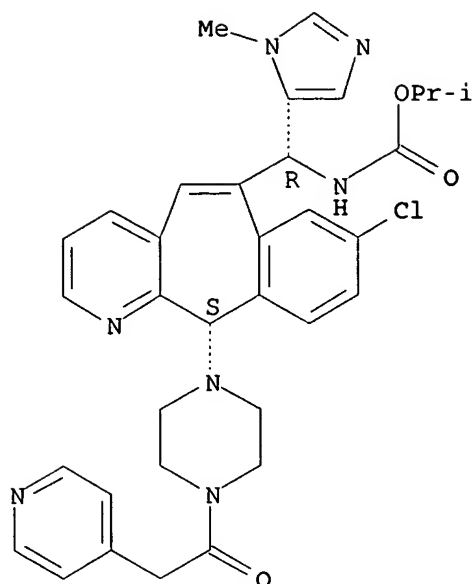
Absolute stereochemistry.



RN 740822-15-5 HCAPLUS

CN Carbamic acid, [(R)-[(11S)-8-chloro-11-[4-(4-pyridinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

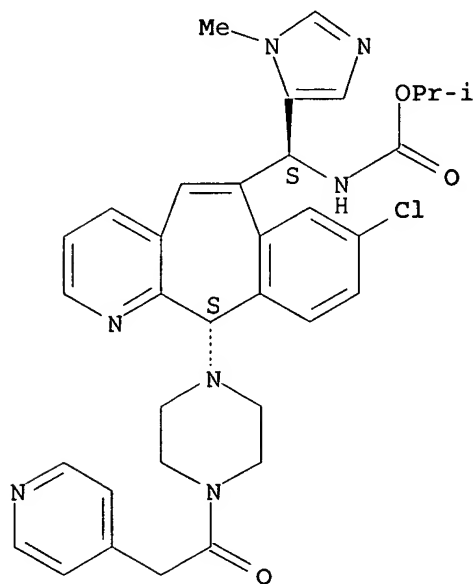
Absolute stereochemistry.



RN 740822-16-6 HCAPLUS

CN Carbamic acid, [(S)-[(11S)-8-chloro-11-[4-(4-pyridinylacetyl)-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

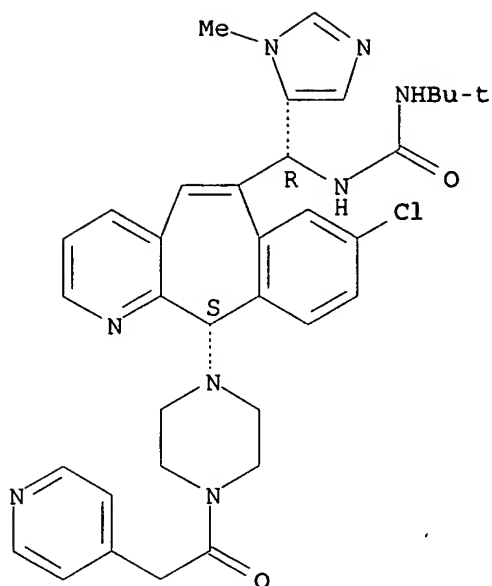
Absolute stereochemistry.



RN 740822-17-7 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

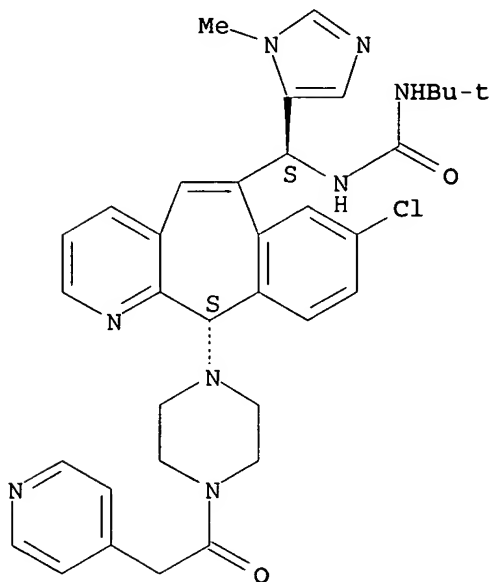
Absolute stereochemistry.



RN 740822-18-8 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

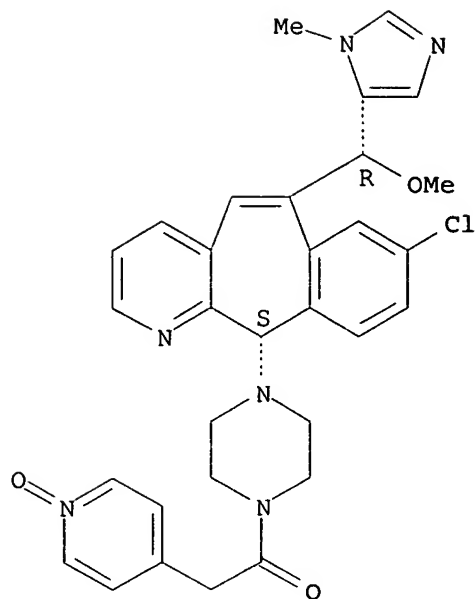
Absolute stereochemistry.



RN 740822-19-9 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

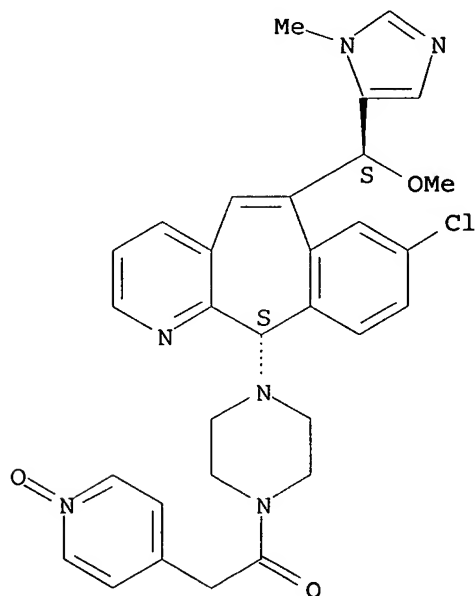
Absolute stereochemistry.



RN 740822-20-2 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

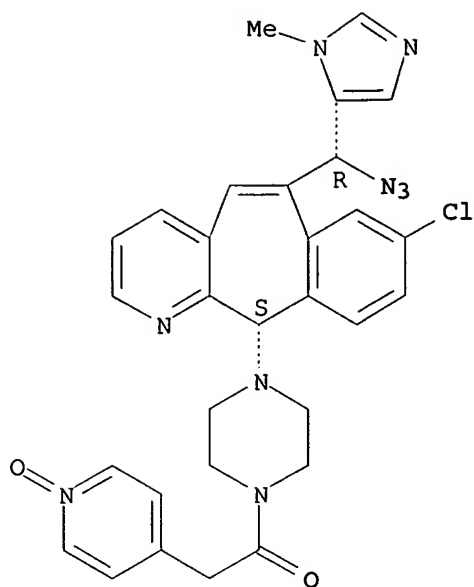
Absolute stereochemistry.



RN 740822-21-3 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(R)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

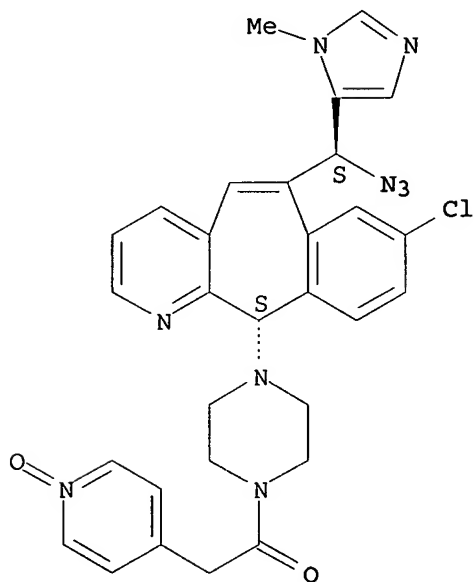
Absolute stereochemistry.



RN 740822-22-4 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(S)-azido(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

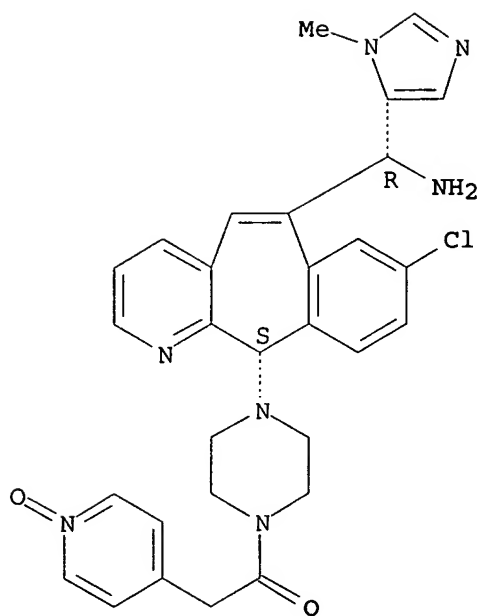
Absolute stereochemistry.



RN 740822-23-5 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(R)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

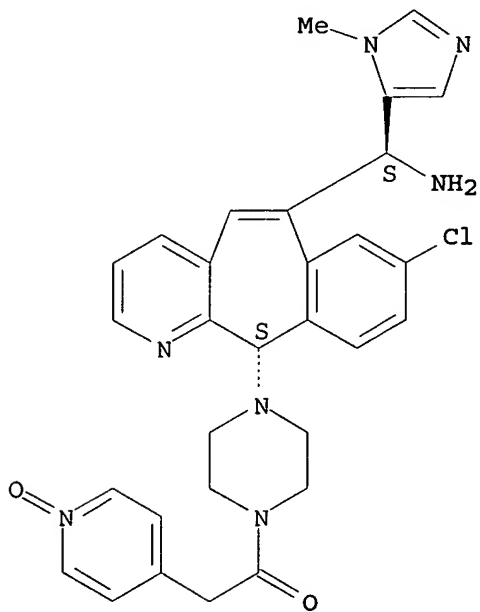
Absolute stereochemistry.



RN 740822-24-6 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(S)-amino(1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

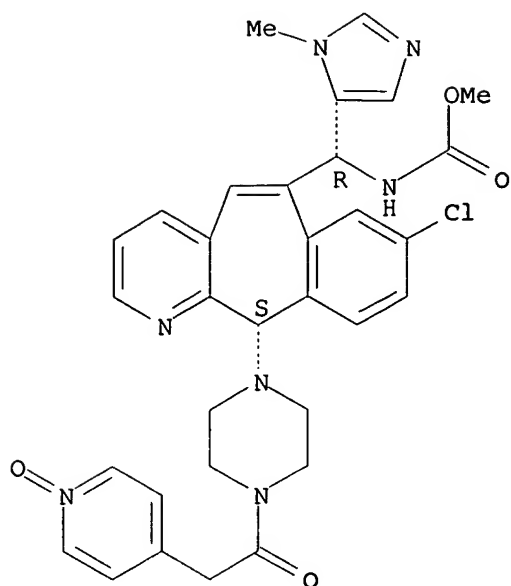
Absolute stereochemistry.



RN 740822-25-7 HCAPLUS

CN Carbamic acid, [(R)-[(11S)-8-chloro-11-[4-[(1-oxido-4-pyridinyl)acetyl]-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

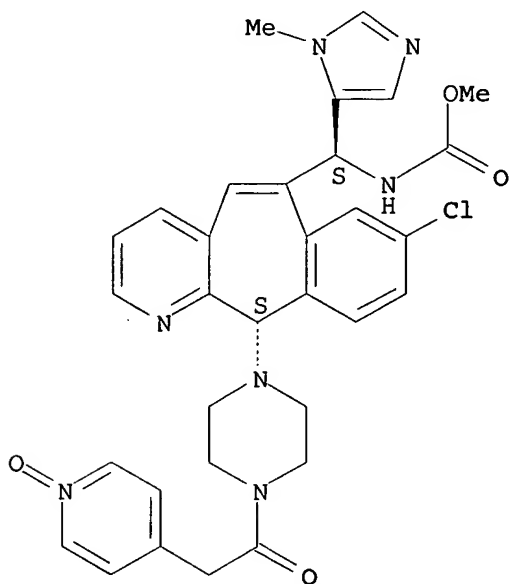
Absolute stereochemistry.



RN 740822-26-8 HCAPLUS

CN Carbamic acid, [(S)-[(11S)-8-chloro-11-[4-[(1-oxido-4-pyridinyl)acetyl]-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl] (1-methyl-1H-imidazol-5-yl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

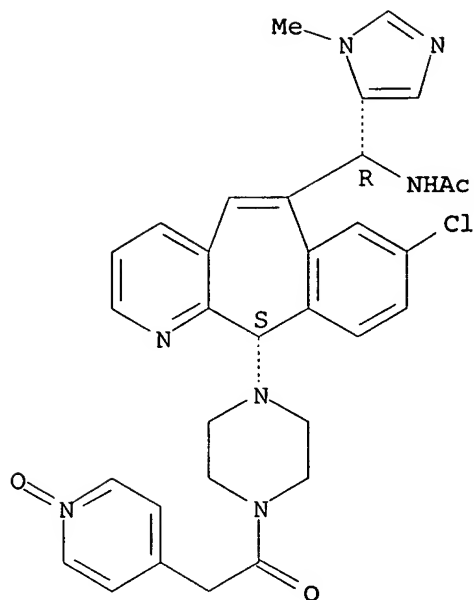
Absolute stereochemistry.



RN 740822-27-9 HCAPLUS

CN Acetamide, N-[(R)-[(11S)-8-chloro-11-[4-[(1-oxido-4-pyridinyl)acetyl]-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl] (1-methyl-1H-imidazol-5-yl)methyl]- (9CI) (CA INDEX NAME)

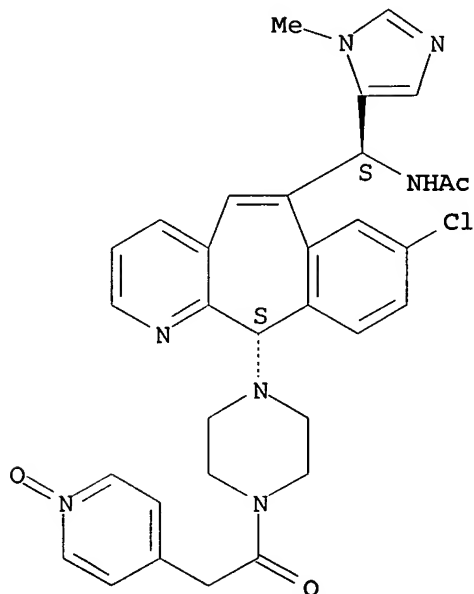
Absolute stereochemistry.



RN 740822-28-0 HCAPLUS

CN Acetamide, N-[(S)-[(11S)-8-chloro-11-[4-[(1-oxido-4-pyridinyl)acetyl]-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-(9CI) (CA INDEX NAME)

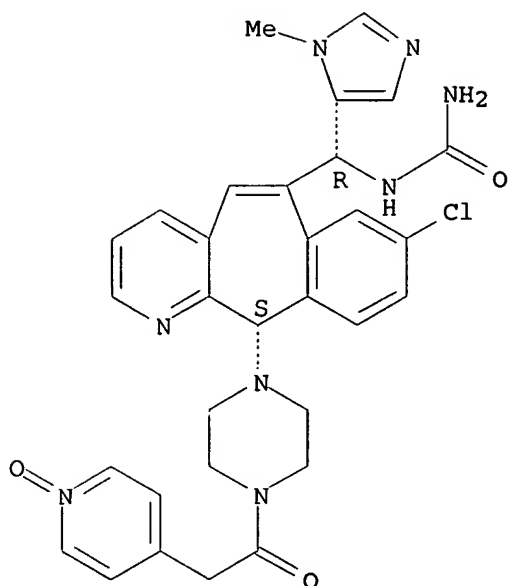
Absolute stereochemistry.



RN 740822-29-1 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(R)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]-(9CI) (CA INDEX NAME)

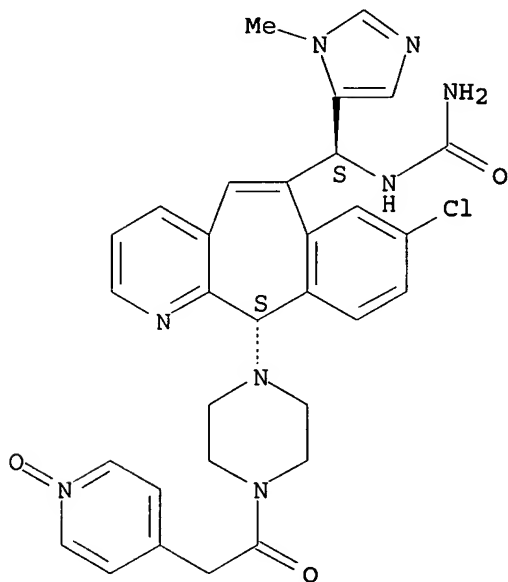
Absolute stereochemistry.



RN 740822-30-4 HCAPLUS

CN Piperazine, 1-[(11S)-6-[(S)-[(aminocarbonyl)amino](1-methyl-1H-imidazol-5-yl)methyl]-8-chloro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]-(9CI) (CA INDEX NAME)

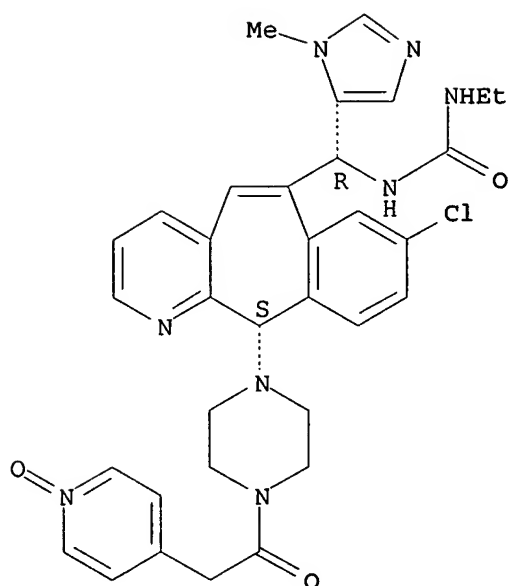
Absolute stereochemistry.



RN 740822-31-5 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]-(9CI) (CA INDEX NAME)

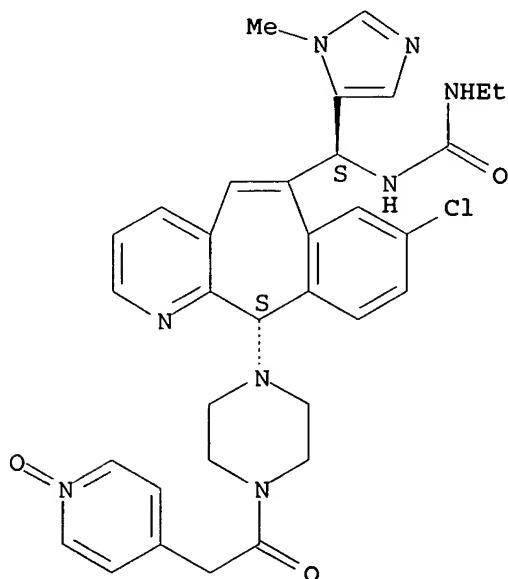
Absolute stereochemistry.



RN 740822-32-6 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-[(ethylamino)carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

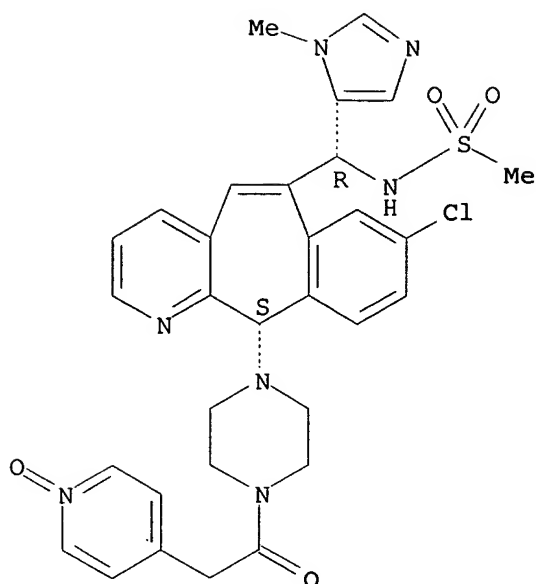
Absolute stereochemistry.



RN 740822-33-7 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[(1-methyl-1H-imidazol-5-yl)[(methylsulfonyl)amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

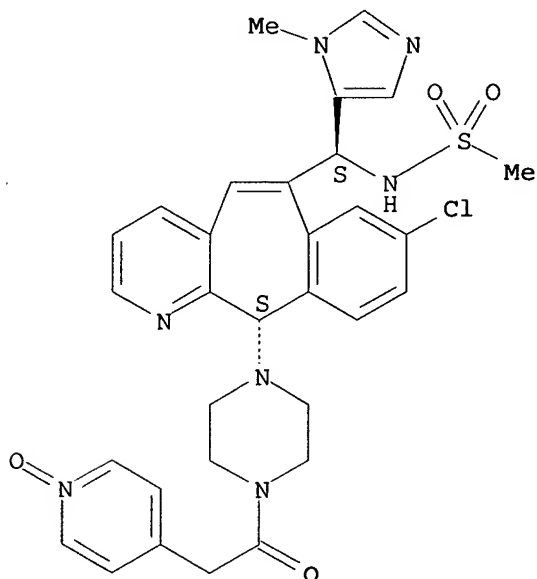
Absolute stereochemistry.



RN 740822-34-8 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-(1-methyl-1H-imidazol-5-yl)[(methylsulfonyl)amino]methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

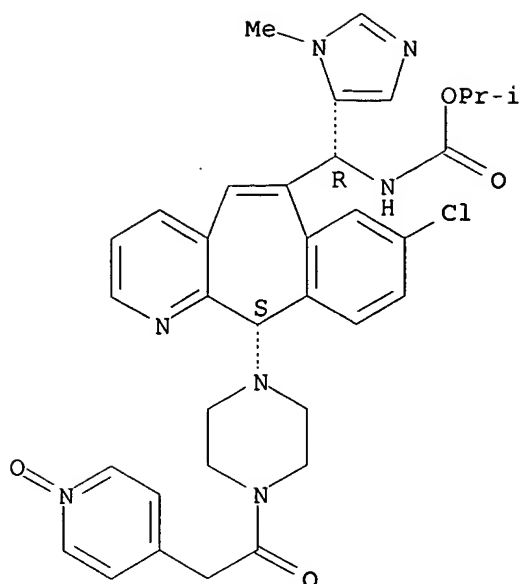
Absolute stereochemistry.



RN 740822-35-9 HCAPLUS

CN Carbamic acid, [(R)-[(11S)-8-chloro-11-[4-[(1-oxido-4-pyridinyl)acetyl]-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

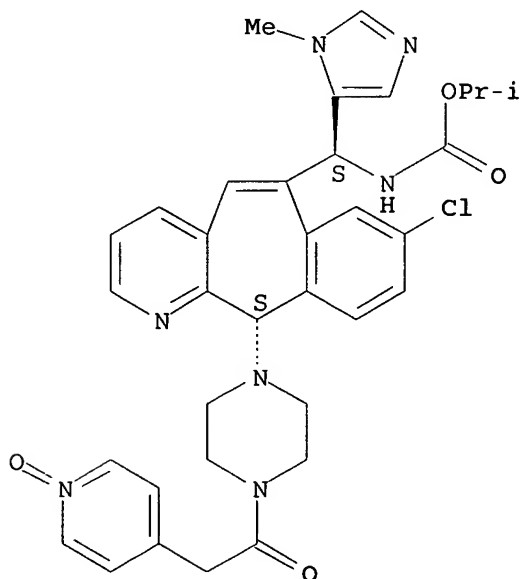
Absolute stereochemistry.



RN 740822-36-0 HCAPLUS

CN Carbamic acid, [(S)-[(11S)-8-chloro-11-[4-[(1-oxido-4-pyridinyl)acetyl]-1-piperazinyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-6-yl](1-methyl-1H-imidazol-5-yl)methyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

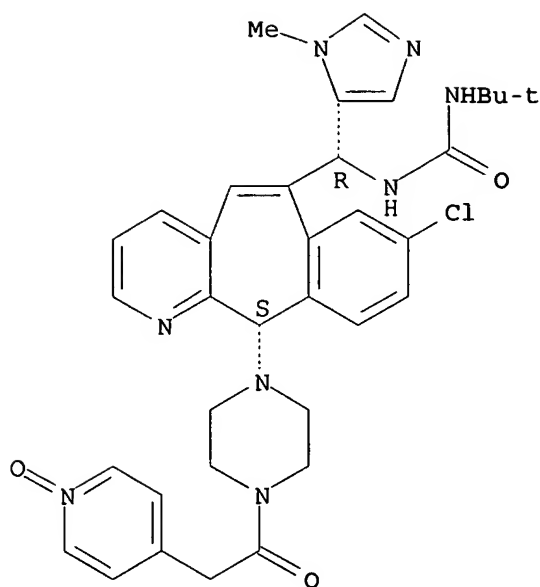
Absolute stereochemistry.



RN 740822-37-1 HCAPLUS

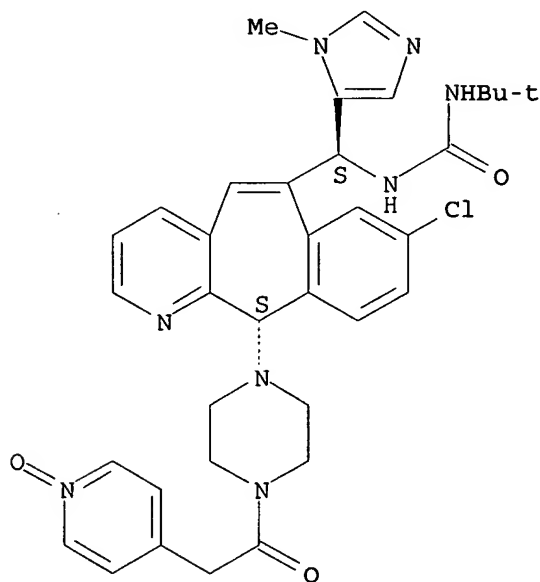
CN Piperazine, 1-[(11S)-8-chloro-6-[(R)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 740822-38-2 HCAPLUS
 CN Piperazine, 1-[(11S)-8-chloro-6-[(S)-[[[(1,1-dimethylethyl)amino]carbonyl]amino](1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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DOCUMENT NUMBER: 141:106498

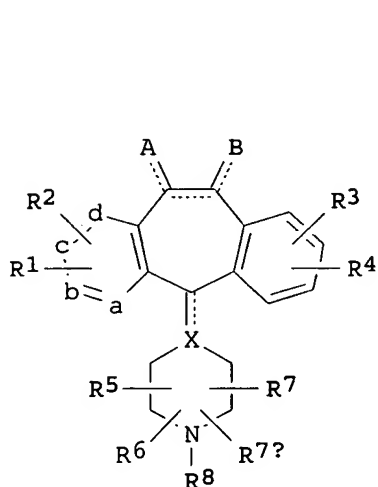
TITLE: Preparation of tricyclic antitumor compounds as farnesyl protein transferase inhibitors

INVENTOR(S): Zhu, Hugh Y.; Njoroge, F. George; Cooper, Alan B.; Guzi, Timothy; Rane, Dinanath F.; Minor, Keith P.; Doll, Ronald J.; Girijavallabhan, Viyyoor M.; Santhanam, Bama; Pinto, Patrick A.; Vibulbhan, Bancha; Keertikar, Kartik M.; Alvarez, Carmen S.; Baldwin,

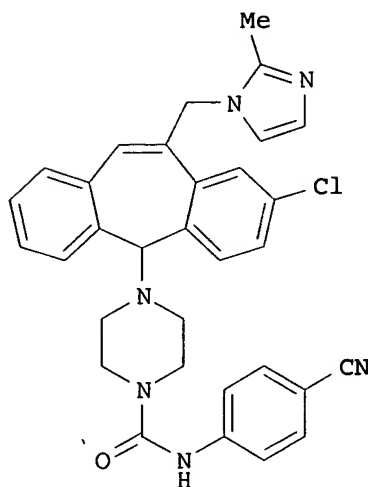
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 Bishop, W. Robert; Wang, James J.-S.; Desai, Jagdish
 A.
 PATENT ASSIGNEE(S): Schering Corporation, USA
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US 2004122018	A1	20040624	US 2002-325896	20021219
US 2002198216	A1	20021226	US 2001-940811	20010828
US 2003229099	A1	20031211	US 2002-85896	20020227
US 2004122018	A1	20040624	US 2002-325896	20021219
PRIORITY APPLN. INFO.:			US 2001-940811	A2 20010828
			US 2002-85896	A2 20020227
			US 2002-325896	A 20021219
			US 2000-229183P	P 20000830

GI



I



II

AB Title benzo[5,6]cyclohepta[1,2-b]pyridines and analogs (I) [wherein one of a, b, d, e = N, N=O; remaining a, b, d, e = C substituted with R1 or R2; or each a, b, d, e = C substituted with R1 or R2; X = N, C, CH; A, B = independently H, (un)substituted R9, carbamoyl(alkyl), amino(alkyl), acylamino(alkyl), ureido(alkyl), etc.; R1-R4 = independently H, halo, CF3, alkoxy, amino, NO2, CN, alkyl, alkenyl, alkynyl, etc.; R5-R7a = independently H, CF3, acyl, alkyl, aryl; R8 = H, alkoxycarbonyl, aryloxycarbonyl, alkylsulfonyl, arylsulfonyl, etc.; R9 = (un)substituted heteroaryl(alkyl), arylalkoxy, heterocyclyl(alkyl), etc.; and stereoisomers, pharmaceutically acceptable salts, solvates, and prodrugs thereof] were prepared as farnesyl protein transferase (FPT) inhibitors. For example, a multi-step synthesis starting from tert-Bu 4-[8-chloro-6-(hydroxymethyl)-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinecarboxylate, 2-methylimidazole, and p-cyanophenyl isocyanate gave (S)-II. The latter inhibited tumor growth of mouse H-Ras fibroblasts, HTB-177 human non-small cell lung cancer cells, and LOX human melanoma cells by 98% (60 MPK, p.o., BID, x2), 96% (80 MPK, p.o., BID, x3), and 90.3% (60 MPK, p.o., BID, x1), resp. Compds. of the invention inhibited FPT activity with IC50 values in the range of 0.05 nM to 100 nM

and suppressed anchorage-independent growth of human tumor cells in a soft agar assay with IC50 values in the range of <0.5 nM to 50 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of proliferative diseases, such as cancer.

IT 721435-94-5P 721435-95-6P 721436-05-1P
721436-06-2P 721437-03-2P 721437-04-3P
721437-14-5P 721437-15-6P 721437-95-2P
721437-96-3P 721438-06-8P 721438-07-9P
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721439-02-7P 721439-82-3P 721439-83-4P
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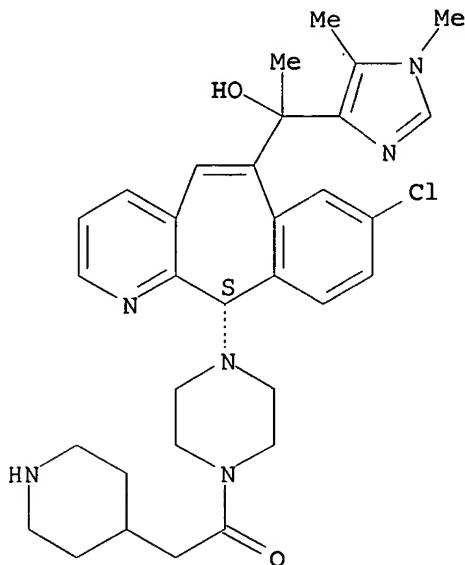
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(FPT inhibitor; preparation of tricyclic antitumor agents as farnesyl protein transferase inhibitors for treatment of cancer and other proliferative diseases)

RN 721435-94-5 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-(1,5-dimethyl-1H-imidazol-4-yl)-1-hydroxyethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

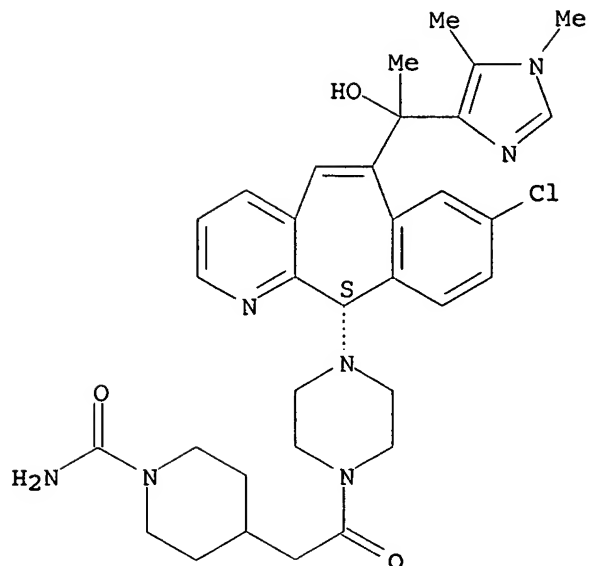
Absolute stereochemistry.



RN 721435-95-6 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[1-(1,5-dimethyl-1H-imidazol-4-yl)-1-hydroxyethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

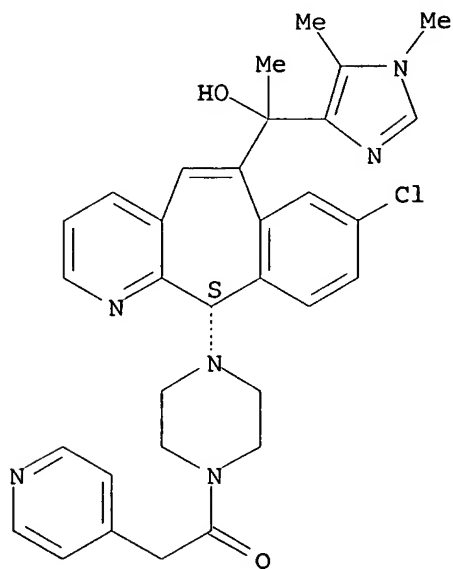
Absolute stereochemistry.



RN 721436-05-1 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-(1,5-dimethyl-1H-imidazol-4-yl)-1-hydroxyethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

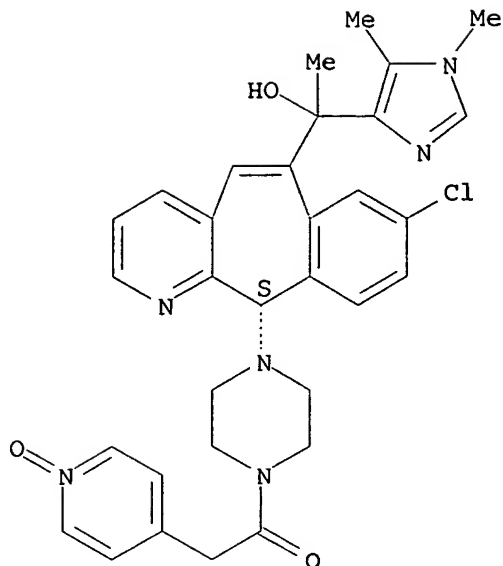
Absolute stereochemistry.



RN 721436-06-2 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-(1,5-dimethyl-1H-imidazol-4-yl)-1-hydroxyethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

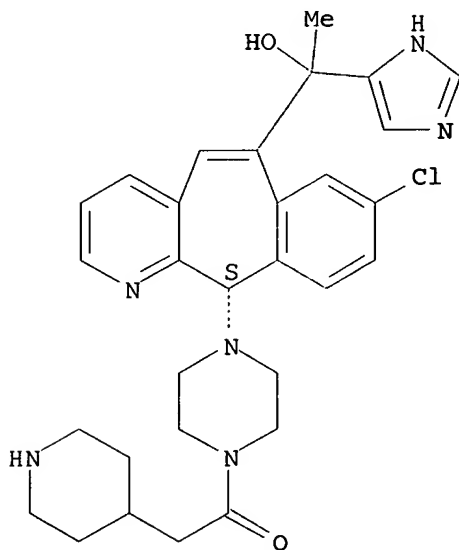
Absolute stereochemistry.



RN 721437-03-2 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI)
(CA INDEX NAME)

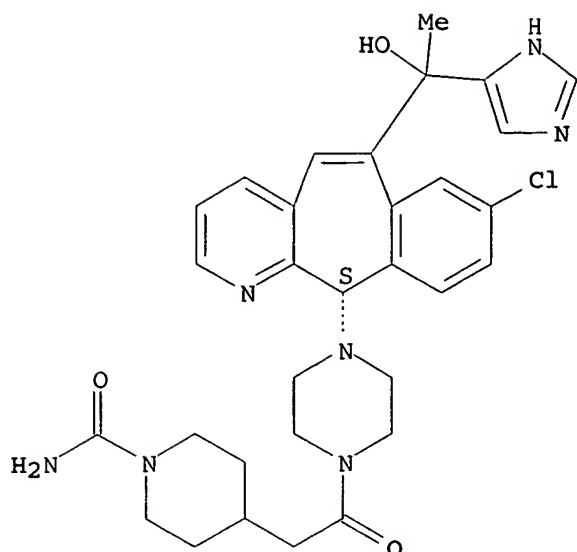
Absolute stereochemistry.



RN 721437-04-3 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[1-hydroxy-1-(1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

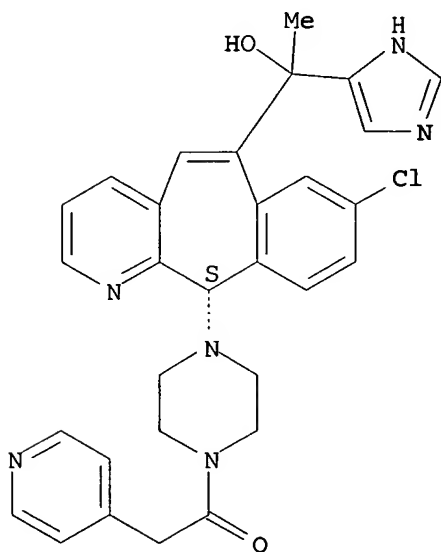
Absolute stereochemistry.



RN 721437-14-5 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI)
(CA INDEX NAME)

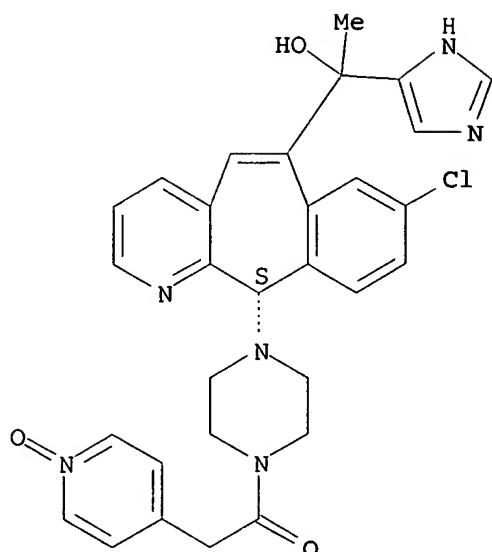
Absolute stereochemistry.



RN 721437-15-6 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI)
(CA INDEX NAME)

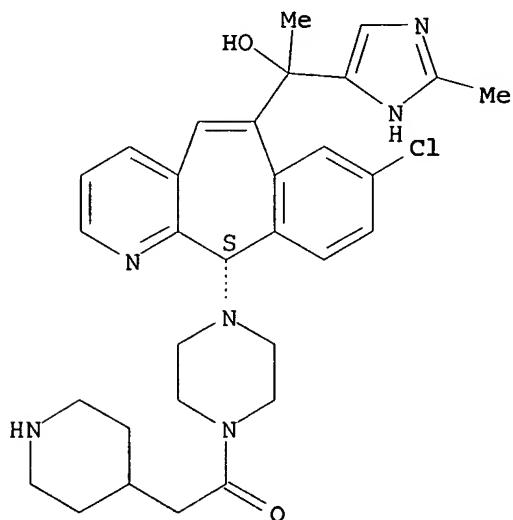
Absolute stereochemistry.



RN 721437-95-2 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(2-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)-(9CI) (CA INDEX NAME)

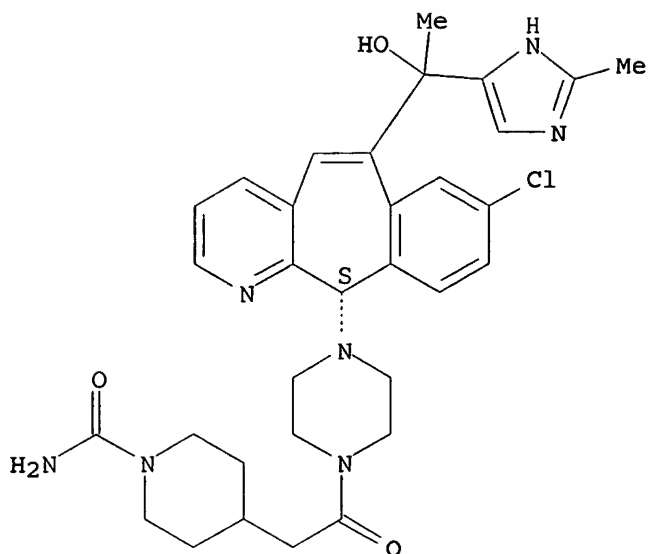
Absolute stereochemistry.



RN 721437-96-3 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[1-hydroxy-1-(2-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

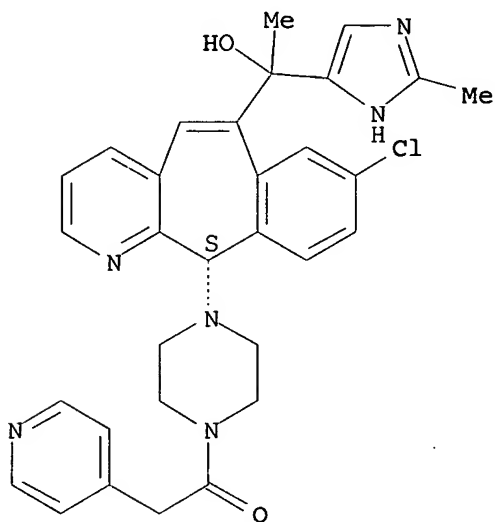
Absolute stereochemistry.



RN 721438-06-8 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(2-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

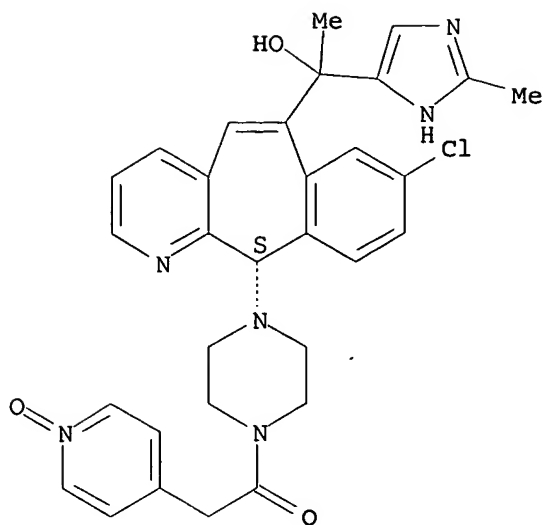
Absolute stereochemistry.



RN 721438-07-9 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(2-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

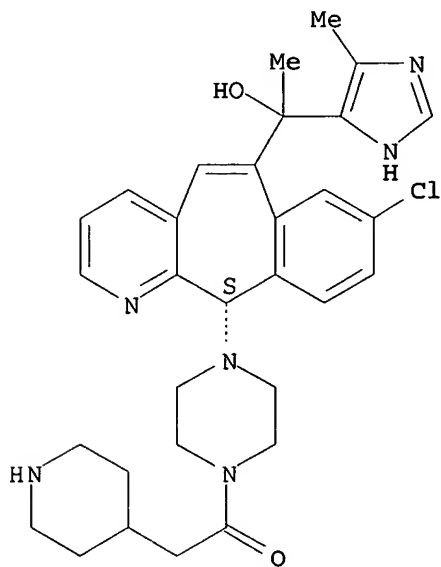
Absolute stereochemistry.



RN 721438-90-0 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(5-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

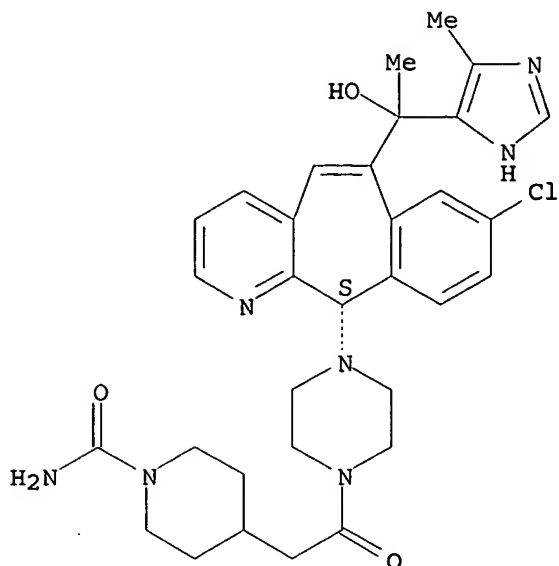
Absolute stereochemistry.



RN 721438-91-1 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[1-hydroxy-1-(5-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

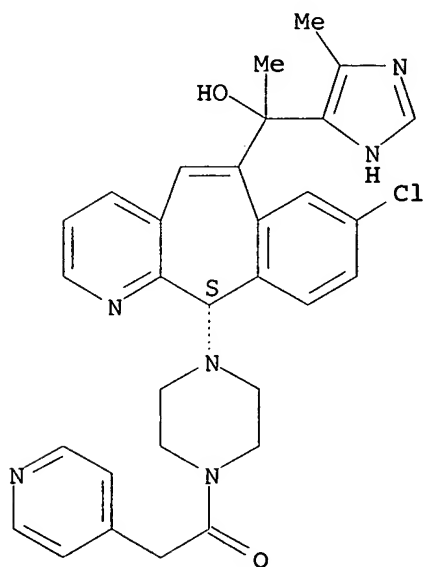
Absolute stereochemistry.



RN 721439-01-6 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(5-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

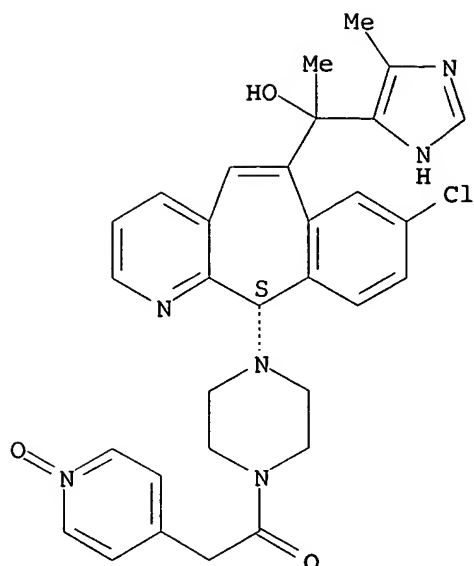
Absolute stereochemistry.



RN 721439-02-7 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-(5-methyl-1H-imidazol-4-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

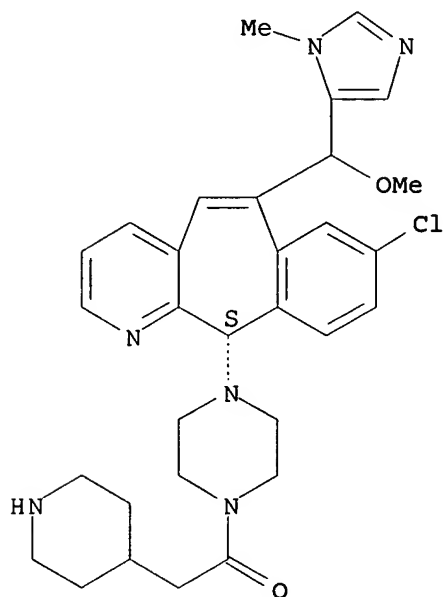
Absolute stereochemistry.



RN 721439-82-3 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)-(9CI) (CA INDEX NAME)

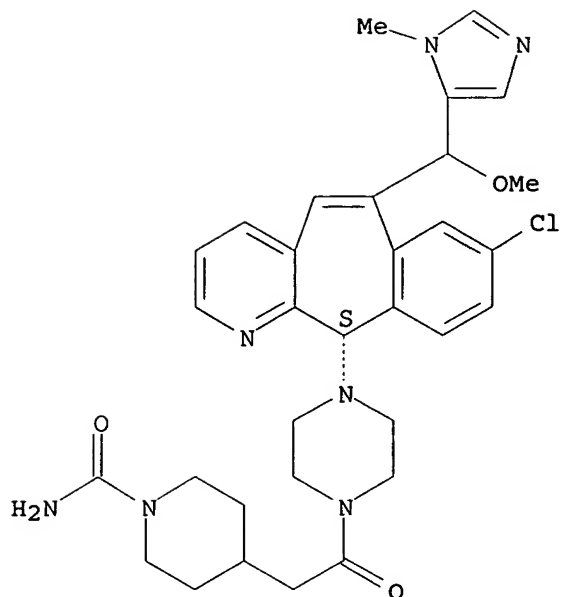
Absolute stereochemistry.



RN 721439-83-4 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]-(9CI) (CA INDEX NAME)

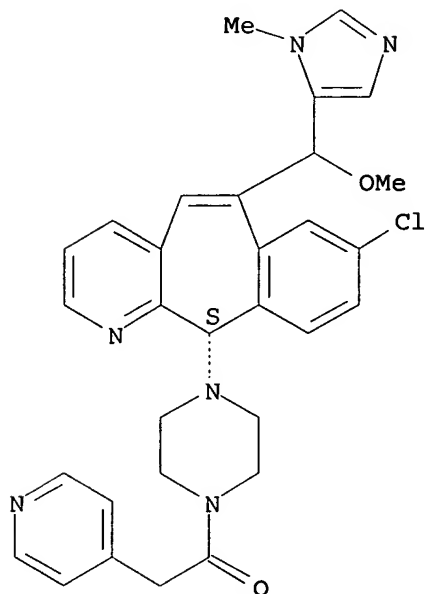
Absolute stereochemistry.



RN 721439-93-6 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI)
(CA INDEX NAME)

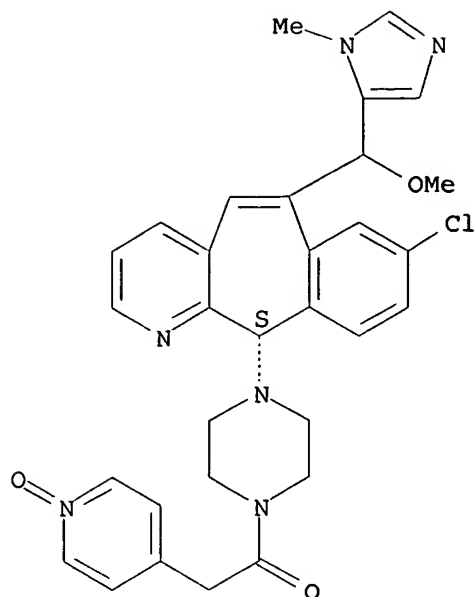
Absolute stereochemistry.



RN 721439-94-7 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[methoxy(1-methyl-1H-imidazol-5-yl)methyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

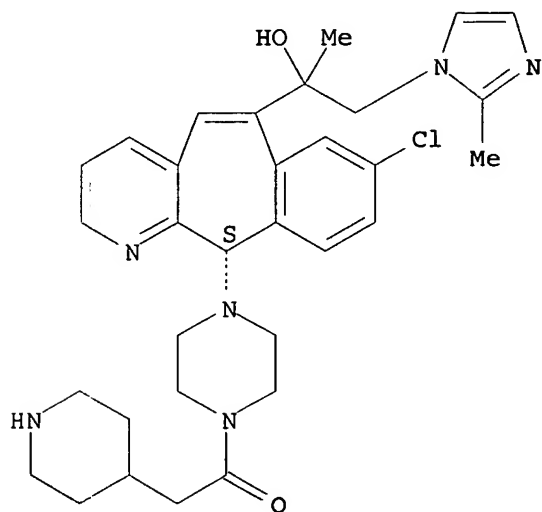
Absolute stereochemistry.



RN 721440-80-8 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-methyl-2-(2-methyl-1H-imidazol-1-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-piperidinylacetyl)- (9CI) (CA INDEX NAME)

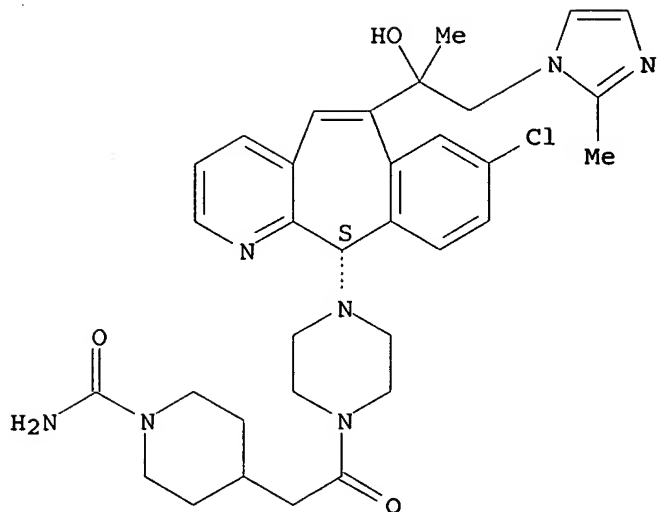
Absolute stereochemistry.



RN 721440-81-9 HCAPLUS

CN 1-Piperidinecarboxamide, 4-[2-[4-[(11S)-8-chloro-6-[1-hydroxy-1-methyl-2-(2-methyl-1H-imidazol-1-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

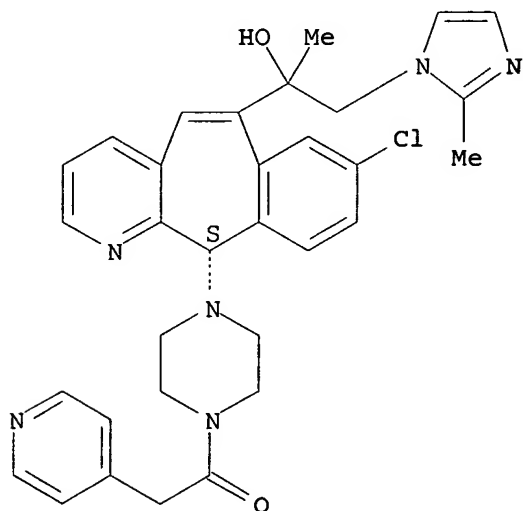
Absolute stereochemistry.



RN 721440-91-1 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-methyl-2-(2-methyl-1H-imidazol-1-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-(4-pyridinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 721440-92-2 HCAPLUS

CN Piperazine, 1-[(11S)-8-chloro-6-[1-hydroxy-1-methyl-2-(2-methyl-1H-imidazol-1-yl)ethyl]-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl]-4-[(1-oxido-4-pyridinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.